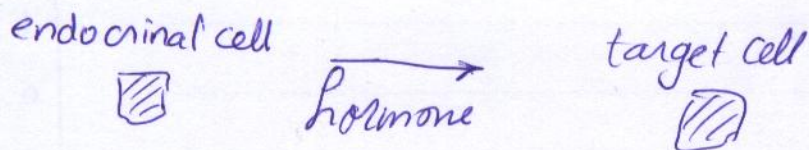


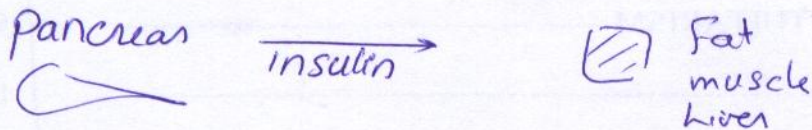
endocrine
 clinical / (سجل) /
 spot diagnosis

Introduction to Endocrine

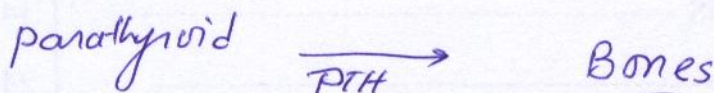
Hormones = Hormone



eg

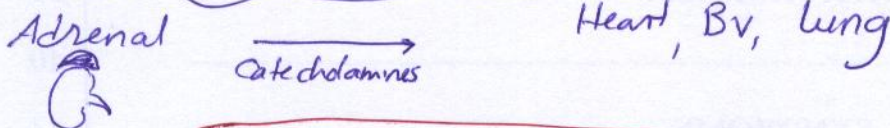


eg



→ hormone: chemical messenger produced from endocrinal cell to act on distant target cell distant from site of production

eg



* TRH

* TSH = thyrotropin

* Hypothalamo-pituitary axis

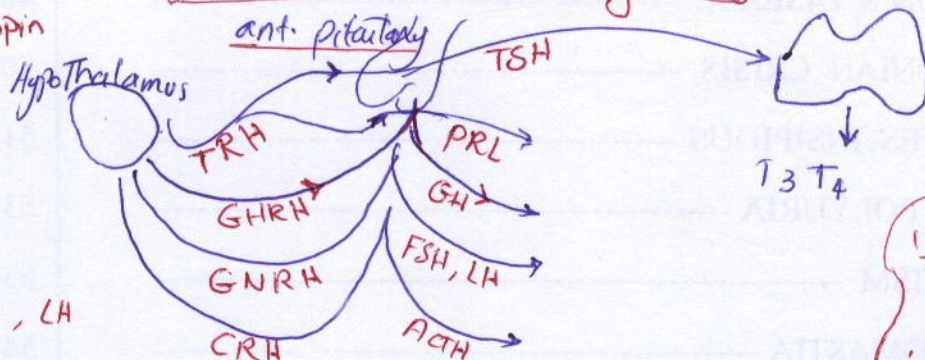
* GHRH → GH

* GnRH → FSH, LH

* CRH = Corticotropin releasing hormone

→ ACTH = Adrenocorticotrophic hormone (on zona fasciculata)

Introduction to thyroid



محور الغدة
 axis

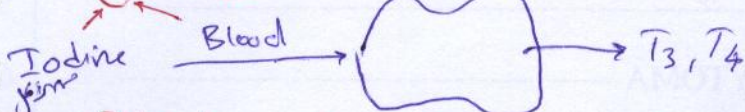
• Pancreas
 • parathyroid

① Trapping [uptake]

2 forms in blood
 * Thyroxin Binding Globulin (TBG)

* free
 free + TBG = Total

free = 0.1% of total
 TBG مفيد مقارنة مع
 لانه free



② Binding = I + Tyrosine = MIT

2I + Tyrosine = DIT

③ Coupling = MIT + DIT = T3 triiodothyronine

DIT + DIT = T4 Tetraiodothyronine

④ storage: T3 & T4 + globulin ⇒ Thyroglobulin

⑤ Release:

splitting → by Protease → free T3, T4 + Globulin

higher control of TSH

(eg)

- T4 > T3 in blood
 - T3 > T4 in potentiality

VISIT...

LANZAROTE
Caliente.COM

↓ growth, Cholesterol ↓, G ↓, Anemia ← T_3, T_4 يقل
 Cholesterol ↓, GT ↑, flushed ← T_3, T_4 زياد

MYXOEDEMA

DEFINITION

- It is a SEVERE form of hypothyroidism.

ETIOLOGY

I. PRIMARY MYXOEDEMA

- The problem is in the thyroid gland itself: "ACQUIRED" or "CONGENITAL"

A) ACQUIRED HYPOTHYROIDISM

1. Inflammation:

"Hashimoto's thyroiditis"

- Autoimmune disease.
- Associated with: thyroid antibodies in 100 % of the cases.
- Associated with: other autoimmune diseases, e.g. PA, SLE, RA, ITP.

2. Idiopathic:

"The most common cause"

- Autoimmune disease. [Atrophic thyroiditis]
- Associated with: thyroid antibodies in 80 % of the cases.
- Associated with: other autoimmune diseases, e.g. PA, SLE, RA, ITP.
- Associated with: thyroid atrophy. Atrophic thyroiditis
- It is probably: the end-stage of Hashimoto's thyroiditis.

3. Iatrogenic:

- Thyroidectomy, excessive Radio-iodine therapy, prolonged use of antithyroid drugs.

4. Irradiation:

- Irradiation for lymphoma may damage the thyroid gland.

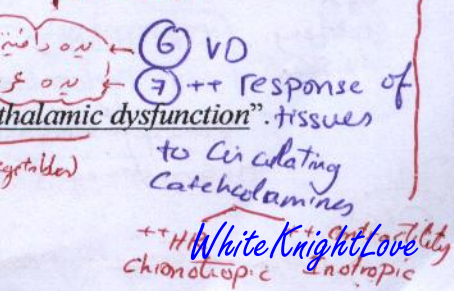
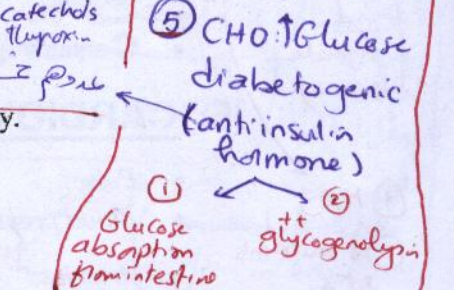
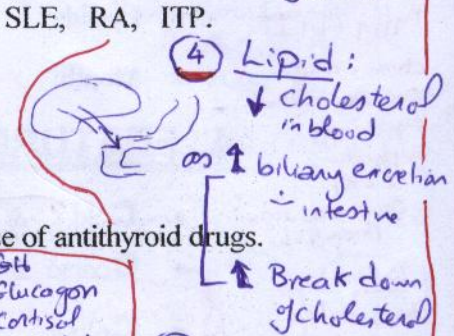
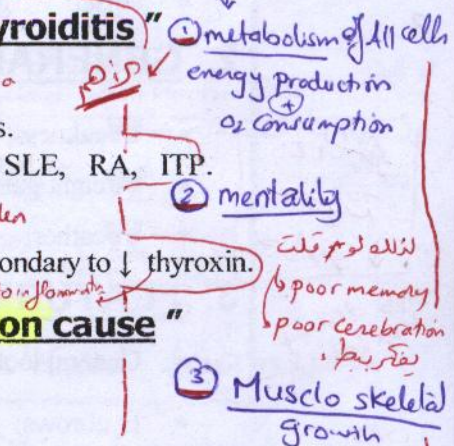
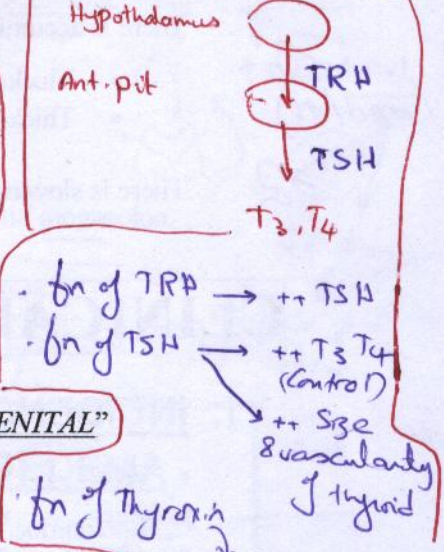
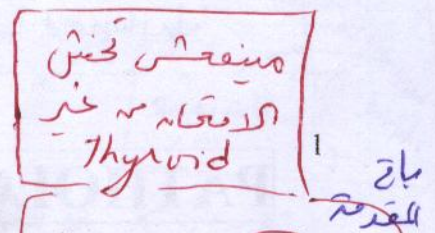
5. Iodine deficiency:

- Endemic myxoedema occurs due to prolonged iodine deficiency.

B) CONGENITAL HYPOTHYROIDISM.

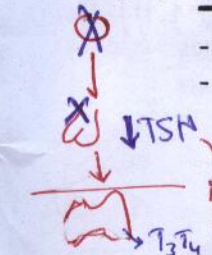
II. SECONDARY MYXOEDEMA

- The problem is not in the thyroid gland itself.
- The problem is suprathyroid: "Pituitary dysfunction" OR "Hypothalamic dysfunction".



Hashimoto MCQ
 دليل
 في رايه
 اول اول
 في رايه
 الكاني
 hashimoto
 وقت
 long standing
 fibrous atrophy

Oral
 Amiodarone
 lithium
 (antipsychotic)



⑦ RBC
 ++ Erythropoietin

⑧ Carotene (vegetables)
 vit A

↓ thyroid → ↓ enzymes activity (w/ metabolic MPS) [↓ catabolism]
 ↓ thyroid → ↓ Excretion of MPS

PATHOLOGY

- There is accumulation of **mucopolysaccharide** in the subcutaneous tissue, leading to:

- Thickening of the skin: nonpitting oedema "**myxoedema**". as
- Thickening of the facial features.

any site (extra cellular)
mainly S.C.

CLINICAL PICTURE

1. INCIDENCE

- Age: 30 - 50 years. (auto immune) < 100% Hashimoto 80% atrophic Abs
- Sex: more common in FEMALES.
- Onset: gradual with delayed symptoms.

2. GENERAL FEATURES

- Weakness**, fatigue. → ↓ Energy production
- Weight gain**, up to obesity, slow movement. → ① ↓ metabolism & ② ↑ deposition of MPS
- Weather**: Intolerance to cold, + hypothermia. → ① ↓ Energy ② obese

3. FEATURES OF THE FACE

- General look**: face is **expressionless** & **bloated**. due to ↓ Energy production in swollen (MPS in cheeks)
- Eyebrows**: sparse with loss of the outer third. → poor response & poor
- Eyelids**: puffy. → hair follicles
- Mouth**: thickened lips & thickened tongue.

4. FEATURES OF THE SKIN

- Cold**, & dry: ↓ heat production (↓ metabolism) → ↓ VC → ↓ HF if occurred → redistribution of blood to heart & brain on exposure of skin
- Coarse** & thickened: decreased sweating → nonpitting oedema "**myxoedema**"
- Colour**: pale due to anemia & yellowish due to deposition of carotene.
- Contains sparse** & brittle hair. → eye brows

5. CARDIOVASCULAR FEATURES

- Pulse**: sinus bradycardia.
- Blood pressure**: secondary hypertension.
- Arteries**: atherosclerosis which may cause CAD.
- Heart**: cardiomegaly due to CM which may end in HF. impending HF
- Pericardium**: pericardial effusion, & may be pleural effusion & ascites.

Polysystoles

MPS → damage of caps → ↑ permeability

Oral

lips → Causes of carotenemia < 2

GRF

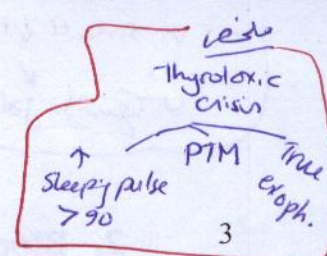
anemia

Macrocytic { 1 ↓ abs. FA/B₁₂
2 ↑ cholesterol
3 associated P.A.
Normocytic (↓ erythropoietin)
Microcytic (Fe²⁺) < menorrhagia malabsorption

White Knight Love

B.P. ↑ : ↑ cholesterol → Atherosclerosis

GRF H.F. in Myxedema: ① DCM (infiltrated by MPS)
② HTN (2nd common cause of HF)
③ CAD (1st common cause of HF)
④ ↓ inotropism



6. GENITAL FEATURES

- Galactorrhoea & Menorrhagia: in females.
- Gynecomastia: in males.

7. GIT FEATURES

- Slow motility → constipation OR myxoedema megacolon.
- Slow absorption → malabsorption.

8. NEUROLOGICAL FEATURES

NEUROLOGICAL FEATURES OF MYXOEDEMA

- Mental impairment:** poor memory, ^{Poor cerebration} slow thinking, somnolence.
- Myxoedema madness:** psychosis, depression. → lazy
- Myxoedema coma.**
- Myopathy & peripheral neuropathy.** → (disturbed neurotransmitter)
- Mucopolysaccharide accumulation:**
 - In the vocal cords → hoarseness of voice.
 - In the internal ear → impaired hearing.
 - In the flexor retinaculum → carpal tunnel syndrome.
- Deep reflexes:** delayed relaxation of deep reflexes. = sustained deep reflex

9. FEATURES OF THE THYROID GLAND

- Enlarged or there is scar of thyroidectomy. ^{hashimoto} ^{iatrogenic}

10. MYXOEDEMA COMA

- Age:** more common in old patients.
- Precipitating factors:** exposure to severe cold, infections.
- Clinical picture:** confusion, then coma with:
 - Hypothermia. ^{no Energy}
 - Hypoventilation. ^[Resp failure]
 - Hypoglycemia.
 - Heart failure.

INVESTIGATIONS

1. Thyroid function tests:

- T3 & T4 (total & free): decreased.
- TSH: increased in primary & decreased in secondary.
- Thyroid radioactive I uptake: decreased.

Increased TSH in primary myxoedema is the most important investigation.

(MCO) Normal levels of TSH will exclude Hypothyroidism (✓)
Normal levels of T3, T4 do not exclude White Knight Love

as v. small $\downarrow T_3 T_4 \rightarrow$ 1 TSH markedly
الحال الجيد $\rightarrow$ الحال الجيد

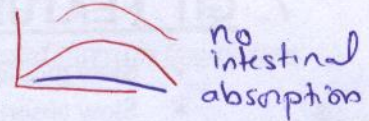
لذلك TSH يفر على حد
نحو $T_3 T_4$ طبع
لذلك، انخفضت افراس جاذبة الغوهاد
TSH و $T_3 T_4$ هو الاهم

2. Blood picture:

- Normocytic anemia: due to BM depression.
- Microcytic anemia: due to iron loss in menorrhagia.
- Macrocytic anemia: due to associated pernicious anemia.

3. Biochemical changes:

- Serum cholesterol: high.
- Serum glucose: flat glucose tolerance curve.
- Serology: thyroid antibodies in Hashimoto's & Idiopathic thyroiditis.
- SGOT & CPK: not specific for myopathy of thyrotoxicosis. may be elevated due to myopathy.



4. ECG:

- Rhythm: -ve chrono Sinus bradycardia.
- Voltage: -ve Tno Low voltage.
- T wave: Flat or inverted T wave. V. non specific

- ① -ve inotropism
- ② pericardial effusion
- ③ DCM
- ④ MPS

DIFFERENTIAL DIAGNOSIS

1. Nephrotic syndrome.
2. Chronic renal failure.
3. Weight gain & obesity.
4. Anemia.
5. Depression.
6. Coma.
7. Polyserositis.
8. Differentiate between primary & secondary myxoedema.

clinical features of Hypothyroidism

$\uparrow TSH$ & $\downarrow T_3 T_4$

& discovered accidentally

follow up every 6M till clinically

V. small doses thyroxin 25-50 ug/d replacement to delay development of hypothyroidism clinically

TREATMENT

"life long"

1. L - thyroxin:

- Start by: 50 ug / day.
- Increase the dose every one month by: 50 ug / day.
- Average maintenance dose: 200 ug / day.
- In old people & in patients with CAD: start by a lower dose (25 ug / day), & the dose is increased very gradually to avoid precipitation of angina & HF.
- Improvement is judged clinically, & by normalization of ECG & cholesterol.

not give 200 from start as +ve in ECG already n. low

HF or angina

2. Treatment of myxoedema coma:

+ Case of comatized

- For Hypothyroidism: IV Hydrocortisone 100 mg / 8 hours.
- For Hypothermia: Gradual rewarming.
- For Hypoventilation: Adequate oxygenation & ventilatory support.
- For Hypoglycemia: Dextrose infusion.
- For Heart failure: ttt of HF. eg digitalis, diuretic

Stroke or IV T_4 500 ug single dose

If T_3 & out the cortisol $\rightarrow$ Sudden severe stimulation of metabolism (stress) of all tissues $\rightarrow$ Cons. of Adrenal reserve

3- Ht of subclinical hypothyroidism:

Acute Addison



DISORDERS OF THE PITUITARY GLAND

I. DISORDERS OF THE ANTERIOR PITUITARY

1. Hyperpituitarism:

Handwritten notes: "Control of TRH" and "دائماً به" (Always to).

Excess secretion of	Disease
GH	Gigantism & Acromegaly
Prolactin	Galactorrhea
ACTH	Cushing's syndrome disease
TSH	Hyperthyroidism
Gonadotropins	Precocious puberty
MSH melanocyte stimulating Hr.	Hyperpigmentation

Handwritten notes: "syndrome of Addison's disease" and "Adrenal" with a drawing of an adrenal gland.

2. Hypopituitarism:

a) In childhood:

Handwritten note: "↓ GH"

- Pituitary dwarfism (Levi-Lorain syndrome).
- Frolich's syndrome.
- Laurance Moon Biedle syndrome.

Handwritten note: "dwarfism"

b) In adults:

Handwritten note: "نادر خط واحد بس يتصل" (Rare, only one line connects).

- Isolated hormonal deficiency:
 - Decreased ACTH → Pituitary Addison's disease.
 - Decreased TSH → Pituitary myxoedema.

Handwritten note: "النشهر كله يتصل" (The whole gland connects).

- Pan Hypopituitarism: (Simmond's disease).
Sheehan's

II. DISORDERS OF THE POSTERIOR PITUITARY

- Decreased ADH → Diabetes insipidus..
- Increased ADH → SIADH.

GIGANTASIM

ETIOLOGY

- Excessive secretion of GH "before fusion of the epiphysis" due to:

- Pituitary hyperplasia: common.
- Pituitary adenoma: rare.

Affecting
Acidophil
cells
GH بنه

Puberty

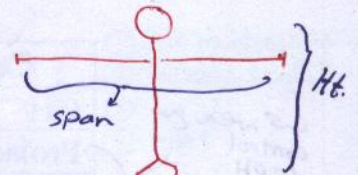
hyperplasia: قاعدة
if long standing
Tumor: قطب

لا ياتي نظري
ولا ياتي clinical
DD. of
Long stature
tall

CLINICAL PICTURE

A) ENDOCRINAL MANIFESTATIONS

1. Disproportionate gigantism: span > height.
2. Later on: features of acromegaly occur.
3. Very late: fatigue & weakness occur due to pituitary insufficiency.



Elong standing
hyperfunction
↓
exhaustion of pit
tissue
or long standing
adenoma
↓
enlarges & destroy
the gland

B) NEUROLOGICAL MANIFESTATIONS

- Refer to "Brain tumours" in Neurology.

"pressure manifestations"

INVESTIGATIONS

- See investigations of Acromegaly.

- 1 - ant
- 2 - post
- 3 - lat
- 4 - above

DIFFERENTIAL DIAGNOSIS

- From other causes of: "TALL STATURE":

1. Familial & racial: proportionate gigantism. (span = height)
2. Primary hypogonadism: Disproportionate gigantism + feminine characters.
3. Marfan's syndrome: Aortic regurge, Mitral Regurge. (MVP)
Dislocation of the lens, Dislocation of the joints.
High arched palate, Arachnodactyly.



↓ sex hormones
(sex hr. needed
for epiphyseal closure)

TREATMENT

- See treatment of Acromegaly.

ACROMEGALY

clinical

ETIOLOGY

- Excessive secretion of GH "after fusion of the epiphysis" due to:

- Pituitary adenoma: common.
- Pituitary hyperplasia: rare.

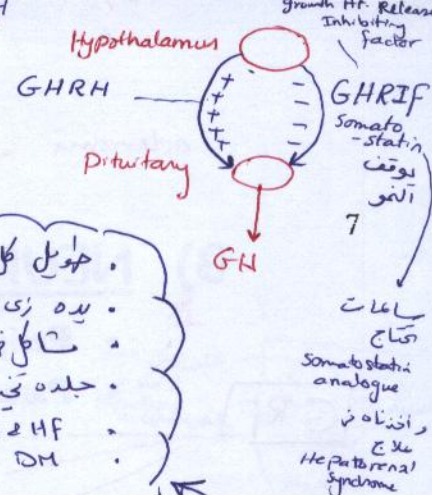
Acidophils

acromegaly

(A) Action of G.H

1. $\uparrow$ Pth: anabolic (body building): growth & develop of all tissues
2. $\uparrow$ Ca $\uparrow$ Pth: $\uparrow$ intestinal absorption (زيادة الامتصاص في الأمعاء)
3. Diabetogenic $\uparrow$ G: $\uparrow$ gluconeogenesis (زيادة إنتاج الجلوكوز)

(B) Control of G.t



CLINICAL PICTURE

- *Age:* 20 – 40 years. ♂ = ♀
- *Onset:* gradual.
- *Course:* slowly progressive.

جلد اول کل حاجت و نہ کثیر
بدہ ری بکلوفا
ساکل فی المشی والحركة
جلد نہ تہ
HTN 2 HF
DM

A) ENDOCRINAL MANIFESTATIONS

Spot Diagnosis

1. **Head & face:**

وہیف منی کوئیس
"Ape-like face"

- **Big skull with elongated face.**
- **Big ears, Big nose, Big lips, Big tongue.**
- **Prognathism + separation of the teeth.** *- as jaw enlarges → w*
- **Prominent frontal bosses & prominent supraprbital ridges.**

protruded
mandible
due to growth

Xray lat view

2. Hands:

“Spade-like hands”

- **Big hands with blunt fingers.**

سقامش مدب
بقر مدب

3. **Skeletal affection:**

- Osteoarthritis may occur. *degenerated cartilage*

① → over growth of bones (destroy cartilage)
② → ↑ wt

- ^{Osteoarthritis} Ligament lax

due to overgrowth of Periapical C.T.
→ stretch of ligaments for long time → (lat)

4. **Skin affection:**

- Thick, wrinkled, greasy.
Overgrowth

→ hypertrophied sebaceous glands

5. Organ enlargement:

- **H**epatosplenomegaly.
- **H**eat enlargement (with *Cardiomyopathy*) → **H**F.
- **H**ypertrophy of the wall of the blood vessels → **H**ypertension.
- **H**ypertrophy of the larynx → **H**oarseness of voice.

دفعاً لارتفاع
تقيس الضغط
الحالة
acromegaly

6. Associated endocrinal disturbances:

- *Diabetes mellitus*: may occur in 30 % of the cases. effect
- *Galactorrhoea*: may occur. $\longrightarrow$ adenoma of pit. $\longrightarrow$ secretes PRL

7. Muscle affection:

- Early: increased muscle power,
- Late: decreased muscle power & *MYOPATHY*

Muscle overgrowth $\rightarrow$ outgrows its blood supply
relative ischemia $\leftarrow$ & already B.V. thickened

adenoma ← Adenoma غالباً Adenoma وحسب لـ hyperplasia لو طول ←

8

B) NEUROLOGICAL MANIFESTATIONS

- **Peripheral neuropathy.** ↑ Growth of interstitial tissue of nerve → thickened
- **Parasthesias in hands & feet may occur due to:**

GRF

- Peripheral neuropathy.
- Diabetic neuropathy. 30%
- Carpal tunnel syndrome. Entrapment neuropathy

- 1 hypertrophy of nerves →
- 2 " of bone
- 3 " of retractor

delayed conduction
تأخر في التوصيل

- **Pressure manifestations:**
- Refer to "Brain tumours" in Neurology.

أشهر
أكثر دواعي
عنه دى ن

INVESTIGATIONS

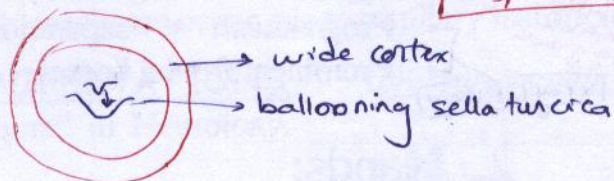
I. IMAGING

1. X-ray:

a) Skull:

- Thick cortex.
- Wide frontal sinuses.
- Prognathism + separation of the teeth.
- Sellar changes: enlargement of the sella turcica.

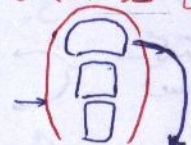
Lat view



b) Hands:

- Phalanges: Broadening of the phalanges.
- Terminal phalanges: Tufting of the terminal phalanges (mushroom-like).

Soft tissue is v. prominent



أشهر الأمراض
metastasi
Acromegaly
Thalassemia
RA
Acromegaly

2. CT & MRI of the skull:

- For accurate diagnosis of pituitary tumours.

للتنقية بجاذب واحدة
معدة
Joint space
if preserved → Acromegaly

II. HORMONES

1. GH level in the serum:

- Increased (normally: < 5 ng/ml in adults).

GH

2. Glucose suppression test:

- IV glucose fails to decrease GH level.

IV Glucose → ↑ glucose in blood

-ve feed

3. Prolactin level in the serum:

- Increased in 30 % of the cases.

دواء
Pit. بقل افراز يفرز النظر
-ve feed

III. BLOOD CHEMISTRY:

- Increased Ca, Increased Phosphates, Increased Glucose.

30 %

TREATMENT

1. Surgical ttt:

- Trans-sphenoidal.
- Trans-frontal

"Removal of the pituitary"

2. Medical ttt:

- Bromocriptine (30 mg / day): $\downarrow$ level of GH & $\downarrow$ size of the tumour.
- Synthetic somatostatin (100 mcg / 8 h): *the drug of choice.*

3. Irradiation of the pituitary:

- If surgical ttt is contraindicated
- If medical ttt gives no response.

4. Symptomatic ttt:

- e.g. for DM & for Hypertension. & Hf

anti diabetic

anti HTN

dopamine also anti parkinsonian
migraine & dopamine antagonist

SS = octreotide
 $\downarrow$ GH release
ACEI ARBs

PAN HYPOPITUITARISM

(Simmond's disease)

ETIOLOGY

1. Post-partum hemorrhage "Sheehan's syndrome":

the most common cause

- Post-partum hemorrhage $\rightarrow$ VC & increased clotting tendency $\rightarrow$ thrombosis of the pituitary vessels $\rightarrow$ pituitary infarction.

2. Pituitary tumours.

chromophobe adenoma
craniopharyngioma

3. Pituitary removal by surgery or pituitary irradiation.

$\rightarrow$ can't proper replacement

CLINICAL PICTURE

I. EARLY FEATURES

- Insidious onset of:

II. DEFICIENCY FEATURES

1. Gonadal deficiency:

a) In females:

$\downarrow$ PRL

$\downarrow$ FSH, LH

- Failure to establish lactation after delivery or infertility.
- Atrophy of the breasts, Amenorrhea.
- Loss of libido, Loss of pubic & axillary hair.

b) In males:

- Impotence.
- Loss of libido, Loss of pubic & axillary hair.

PRL TSH GH FSH ACTH LH

ϕ more common

Triad
weakness & apathy & wt. loss

$\downarrow$ ACTH

$\downarrow$ TSH
($\downarrow$ T₃ T₄)
(myxoedema)

$\downarrow$ GH if
wt loss $\leftarrow$ $\downarrow$ GH $\rightarrow$ $\downarrow$ TSH
wt gain $\leftarrow$ $\downarrow$ GH $\leftarrow$ $\downarrow$ TSH
no change $\leftarrow$ $\downarrow$ GH = $\downarrow$ TSH

wt loss

breast & hair normal
Anorexia nervosa

Oral
Adrenal failure
فشل الغدة الكظرية

↓ TSH

↓ ACTH

2. Thyroidal deficiency:

- Clinical features of myxoedema.

"Secondary myxoedema"

عندما يكون هناك قصور في الغدة الدرقية
توضيح: إذا كان هناك قصور في الغدة الدرقية
فإنه يسمى قصور الغدة الدرقية الثانوي
مثال: TSH ↓

3. Adrenocortical insufficiency:

"Secondary adrenal failure"

- Clinical features of Addison's disease,

BUT:

- Hyperpigmentation: is absent.
- Hypotension: is not severe due to continued release of aldosterone.

ACTH

adrenal cortex
ery adrenal failure

4. Pressure manifestations:

- In case of pituitary tumours.

لو كان هناك ورم في الغدة النخامية

Addison's disease
فشل الغدة الكظرية

II. LATE FEATURES

COMA may occur in late stages due to:

- Hypothermia.
- Hypoglycemia.

(↓ TSH) → Myxedema Coma

↓ TSH, ↓ GH, ↓ ACTH → Hypoglycemic Coma

INVESTIGATIONS

1. IMAGING

- X-ray sella turcica.
- CT & MRI of the brain.

2. HORMONES

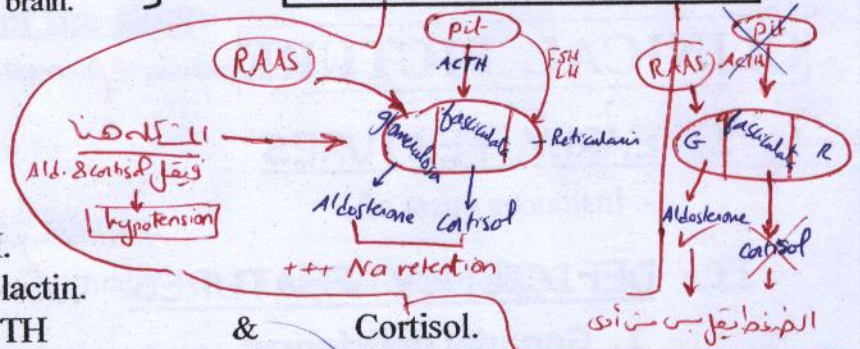
A) ASSAY:

- Decreased GH.
 - Decreased Prolactin.
 - Decreased ACTH
 - Decreased TSH
 - Decreased Gonadotrophins
- & Cortisol.
& T3 & T4.
& Sex hormones.

B) COMBINED INSULIN TOLERANCE TEST:

- Give: IV INSULIN, followed by TRH & GnRH.
- Normally: marked ↑ in GH, ACTH, TSH, Prolactin, FSH, LH.
- In Pan hypopituitarism: no increase in these hormones.

Evidence of Pituitary tumour



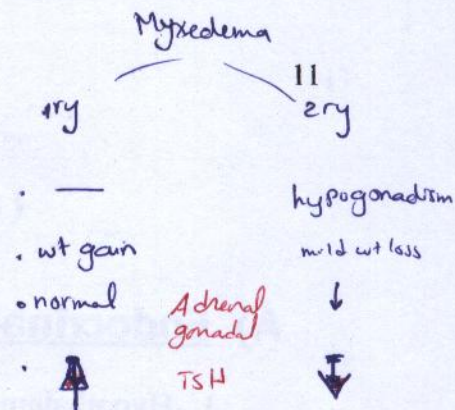
selective ↓
TSH cortisol gonadal

DIFFERENTIAL DIAGNOSIS

1. Primary myxoedema:

"Thyroid myxoedema"

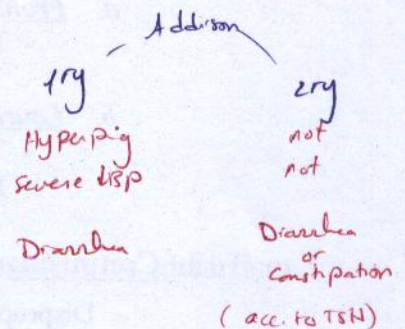
- Features of myxoedema.
- Hypogonadism: absent.
- Body weight: markedly increased.
- Investigations:
 - Gonadal & Adrenal functions: normal.
 - TSH: high.



2. Primary adrenal failure:

"Addison's disease"

- Features of Addison's disease.
- Hyperpigmentation & Hypotension.
- Diarrhoea.
- Investigations:
 - Gonadal & Thyroid functions: normal.
 - ACTH: high.
 - ACTH administration: no effect.



3. Anorexia nervosa:

- It usually occurs in: YOUNG WOMEN.
- ANOREXIA + marked loss of weight.
- AMENORRHEA + normal axillary & pubic hair.
- Breasts are well developed.
- Thyroxin & cortisol levels are NORMAL.

الفقر
Sheehan

4. Primary hypogonadism in males:

- Features of hypogonadism.
 - Disproportionate gigantism: if the condition starts in childhood.
 - Thyroxin & cortisol levels are NORMAL.
- Handwritten notes: "↓ sex hr. w is needed to close ep.phys." (circled), "heart size" (circled).

TREATMENT

1. Treatment of the cause, if possible.

الفقر

2. Hydrocortisone: 30 mg / day.

3. Thyroxin:

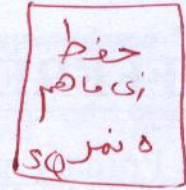
- It should be given after hydrocortisone, to avoid acute adrenal insufficiency.
- It should be given in a small dose, followed by very gradual increase of the dose.

4. Gonadal hormones:

- In females: diethylstilbestrol.
- In males: methyl testosterone.

DWARFISM

(Stunted growth - - Short stature)



A) Endocrinal diseases

1. Hypothalamic syndromes:

a. Frohlich's syndrome:

- Trunkal obesity, hypogonadism, genu-valgum.

b. Laurance Moon Biedle syndrome:

- Trunkal obesity, hypogonadism, genu-valgum.
- Polydactyly, mental retardation, retinitis pigmentosa.

2. Cretinism:

- Disproportionate dwarfism + features of cretinism.

3. Pituitary dwarfism

“ Levi-Lorain syndrome ”

- Proportionate dwarfism + hypogonadism.

4. Precocious puberty:

- Increased secretion of sex hormones causes premature fusion of the epiphysis.

5. IDDM.

B) Severe chronic illness during childhood

1. Cardiac: Congenital, Rheumatic valvular.

2. Chest: Cystic fibrosis, Severe bronchial asthma.

3. Liver: Lipid & glycogen storage disease, Veno-occlusive disease.

4. GIT: Malnutrition, Malabsorption.

5. Renal: Chronic renal failure.

6. Blood: Chronic severe anemia.

7. Chronic infections: e.g. TB.

C) Skeletal causes

1. Achondroplasia:

- Limbs: Short.
- Trunk: Normal.

2. Osteochondrodystrophy:

- Limbs: Short & deformed.
- Trunk: Short & deformed.

3. Osteogenesis imperfecta:

- BONES: Fragile bones → multiple fractures → malunion → dwarfism.
- EYES: Blue sclera.
- EARS: Conductive deafness.

4. Rickets.

5. Pott's disease of the spine.

D) Genetic diseases

1. Laurant Moon Biedle syndrome.

2. Mongolism.

3. Turner's syndrome: primary amenorrhea, sexual infantilism, short stature.

4. Progeria: premature senility.

E) Familial & racial.

1. Breath: Rapid deep breathing (Kussmaul's)
2. Brain: Confusion, then Coma.

TREATMENT

- IV sodium bicarbonate.

Hyperparathyroidism is not the only cause of HCA

* functions of Ca:

1. Ms contraction (actin over myosin)
2. Neuromuscular transmission
3. Bone & teeth
4. Coagulation system

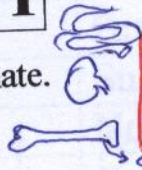
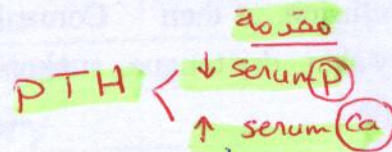
* Normal Levels

total Ca : 8.5 - 10.5 mg/dl
P : 2.5 - 4.5 mg/dl

- * ↑ Ca & ↑ P = Acromegaly
- * ↓ Ca & ↓ P = malabsorption

نمیتواند که الحاحات را برطرف کند
ده تزوید و العکس

albumin ↓
nephrotic syndrome
serum Ca normal
also Albumin must be normal



1. intestine: ↑ absorption (act. vit D)
2. Kidney: ↑ reabsorption, & ↑ excretion of P
3. Bone: ↑ resorption (↑ osteoclastic activity)

control # vit D
so, ↓ serum Ca

if pH normal → 50% ionized
50% non "

if pH ↑ (alkalosis) → ionized ↓

if pH ↓ (acidosis) → ionized ↑

pH
ماده شیمیایی
total
(لا یونی)

shift
ionized
& non "

ionized 50%

nonionized 50%

40%

Pln Bound
(on Albumin)

10%

inorganic

Ca phosphate

Ca citrate

IBD, OM, parathyroid
→ Kid & Gall stones

مقدار کل کلسیم
Total Ca
ماده لو Alb

HYPERPARATHYROIDISM

ETIOLOGY

1. Primary Hyperparathyroidism

- It is due to parathyroid **adenoma** (single OR multiple).
- Serum Ca & PTH: **increased.** → 1st PTH ↑, 2nd Ca ↑

2. Secondary Hyperparathyroidism

- It is a compensatory **hyperplasia** of the parathyroid due to hypocalcemia.
- It results in increased secretion of PARATHORMONE (PTH).
- It returns to normal after treating the cause of hypocalcemia (e.g. CRF or malabsorption).
- Serum Ca & PTH: **increased. PTH, low or normal Ca.**

3. Tertiary Hyperparathyroidism

- It is an irreversible parathyroid hyperplasia (**Tumour**) after longstanding 2ry hyperparathyroidism.
- Serum Ca & PTH: **increased.**

4. Paramalignant syndrome

- It is associated with increased secretion of PTH from an **ectopic tumour** (e.g. bronchial carcinoma).
- Serum Ca & PTH: **increased.**

CLINICAL PICTURE

I. SKELETAL MANIFESTATIONS

1. Bony pains & backache. (spongy → neck femur spine)
2. Pathological fractures.
3. Osteitis fibrosa cystica: **soft, weak, deformed & replaced by** fibrous tissue, multiple cysts on surface of bone.

II. EXTRA-SKELETAL MANIFESTATIONS

1. Renal:

- Polyuria: because hypercalcemia will make the renal tubules less sensitive to ADH.
- Renal stones: multiple, bilateral, recurrent until correction of hypercalcemia.
- Renal calcification: **nephrocalcinosis** occurs in the renal parenchyma & may end in CRF.

2. CVS:

arrhythmias, hypertension, bradycardia, short QT

3. CNS:

apathy, hypotonia, weakness, (sliding of actin & myosin, spasm)

4. GIT:

anorexia, nausea, vomiting, constipation, pancreatitis.

5. Skin:

itching.

6. Eye:

conjunctivitis & keratitis.

7. Hypercalcemic crisis:

8. Metastatic calcification in soft tissues,

e.g. arteries.

9. Gallstones

due to ↑ bile flow, Ca deposition in biliary system due to

10. Kidney stones

due to ↑ Ca deposition in biliary system due to

11. Accelerates atherosclerosis

12. Premature activation of trypsinogen to trypsin → autodigestion (injury)

13. Pancreatic calcification

14. White Knight Love

15. CRF

16. CRF

17. CRF

18. CRF

19. CRF

20. CRF

21. CRF

22. CRF

23. CRF

24. CRF

25. CRF

26. CRF

27. CRF

28. CRF

29. CRF

30. CRF

31. CRF

32. CRF

33. CRF

34. CRF

35. CRF

36. CRF

37. CRF

38. CRF

39. CRF

40. CRF

41. CRF

42. CRF

43. CRF

44. CRF

45. CRF

46. CRF

47. CRF

48. CRF

49. CRF

50. CRF

51. CRF

52. CRF

53. CRF

54. CRF

55. CRF

56. CRF

57. CRF

58. CRF

59. CRF

60. CRF

61. CRF

62. CRF

63. CRF

64. CRF

65. CRF

66. CRF

67. CRF

68. CRF

69. CRF

70. CRF

71. CRF

72. CRF

73. CRF

74. CRF

75. CRF

76. CRF

77. CRF

78. CRF

79. CRF

80. CRF

81. CRF

82. CRF

83. CRF

84. CRF

85. CRF

86. CRF

87. CRF

88. CRF

89. CRF

90. CRF

91. CRF

92. CRF

93. CRF

94. CRF

95. CRF

96. CRF

97. CRF

98. CRF

99. CRF

100. CRF

INVESTIGATIONS

A) CHEMISTRY

1. Blood chemistry:

- Increased Calcium, Decreased Phosphate, Increased Alkaline Phosphatase.

2. Urine analysis:

- Increased Calcium, Increased Phosphate, Increased volume.

not specific
as ↑ in any bone
damage eg: Paget of bone³⁸

1ry, tertiary, PMS

↑ bone turnover

Increased osteocalcin → >30 King Arms strong
(phosphorus)

PTH ↑↑↑ Ph. loss

nephrogenic DI

B) HORMONES

3. Hormonal assay:

- Increased level of PARATHORMONE.

4. Steroid suppression test:

- Normally: Corticosteroids lower the serum Calcium by inhibiting vitamin D.
- In disease: Hydrocortisone 40 mg / 8 hours for 10 days will lower the serum Calcium:

i. In Hypercalcemic states. all other causes

ii. Not in Hyperparathyroidism.

as cortisol only inhibits intestine absorption
bone is not suppressed

C) IMAGING

5. Imaging to localize the parathyroid adenoma:

a) Ultrasonography, CT, MRI.

b) Radio-isotope subtraction scan: digital subtraction imaging

- The neck is imaged during successive injections of 2 radioactive isotopes:

- Thallium: is taken up BOTH by the thyroid & parathyroid.
- Technetium: is taken up ONLY by the thyroid.

- Then image subtraction is done by the computer: → a parathyroid image.

6. Imaging for the clinical manifestations:

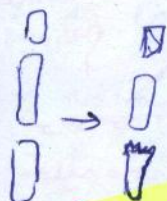
"X-ray"

a) For the bone:

- Absence of the lamina dura around the teeth.
- Bone cysts. (Howship's Lacunae)
- Cod-fish spine: indentation of the vertebral bodies by intervertebral discs.
- Decalcification: ground glass appearance of the bones.
- Erosion: sub-periosteal erosion of the phalanges.
- Pepper-pot skull: mottling of the skull.
- Densitometry: DEXA, plain xray CT

b) For the urinary system:

- Renal stones.
- Renal calcification: nephrocalcinosis.



Spizelli RA.

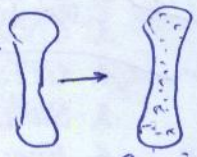
Localized opacity

general diffuse opacity

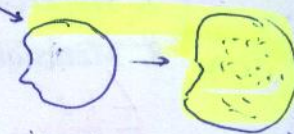
hand layer around sockets



will disc appear like soft bone



newly



White Knight Love

Q: Causes of Hypercalcemia

39

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

1. ENDOCRINAL CAUSES

- a) **Hyperparathyroidism:** primary, tertiary, paramalignant syndrome. (all except 2nd)
- b) **Hyperthyroidism:** not suppressed by cortisol
- * c) **Addison's disease:** ↑ intestinal absorption, ↑ bone turn over.
- d) **Acromegaly:** ↓ cortisol → no inhibition of ↑ intestinal absorption

2. IATROGENIC

- a) Hypervitaminosis D.
- b) Calcium.
- c) Diuretics:
- d) Milk-alkali syndrome.

thiazides & furosemide

pt. peptic ulcer & excess ingestion of milk antacid (for H+) → ↑ Ca → constipation, alkalosis

3. MALIGNANCY

- a) Osteolytic metastasis:
- b) PTH secretion:
- c) Prolonged immobilization:
- d) Activation of Vitamin D:

it causes hypercalcemia due to:

& production of osteoclastic factors. in cases of ectopic tumours, e.g. bronchial carcinoma. in terminal cases. (osteoporosis development as in Lymphoma & multiple myeloma)

4. MISCELLANEOUS

- * a) Sarcoidosis. activation of vit D
- * b) Multiple myeloma.
- c) Prolonged immobilization.
- d) Familial hypocalcemic hypercalcemia: a hereditary disease with ↑↑ tubular Ca reabsorption.

↓ Ca - urine
↑↑ Ca - Blood

TREATMENT

I. Surgery:

- Surgical removal of adenomas.
- Surgical removal of most of the hyperplastic tissue in hyperplasia + ttt of the cause.
- Calcium may be needed after surgery. (as osteoblast & RLN injury may occur)

II. Treatment of acute hypercalcemia:

"Hypercalcemic crisis"

- It is an emergency leading to:

- Nausea, vomiting, abdominal pain.
- Polyuria, dehydration, fever.
- Confusion, coma, death.

- It needs immediate ttt which is life saving:

- IV saline: 4 litres / day for 3 days to correct dehydration & wash out Calcium.
- Chelation: IV Biphosphonate (50 mg IV over 5 h), IV Mithramycin (25 mcg IV over 6 h).
- Calcitonin: (from parathyroid glands) 200 U / 6 hours IV.
- Prednisolone: 1 mg / Kg / day.
- Hemodialysis: in severe cases.

Metabolic encephalopathy

↓ bone resorption
↑ blast (Bazily)
↓ clast
↑ Ca excretion

all causes of hypercalcemia except Hyperpar

Oral why? → ↓ Ca serum
How? → by inhibit vit D
when? → in all causes except Hyperpar

- 1 Addison
- 2 Sarcoidosis
- 3 Multiple myeloma

White Knight Love

TETANY

DEFINITION

- Increased excitability of the nerve & muscle.

ETIOLOGY

Parasthesia
twitches
spasm
convulsions

I. HYPOCALCEMIA

1. Decreased production of Calcium:

"Hypoparathyroidism"

- Congenital: absence. — rare
- Surgical: removal during thyroidectomy.
- Autoimmune. — rare

2. Decreased intake of Calcium:

- Prolonged starvation, anorexia.

3. Decreased absorption of Calcium:

- Malabsorption syndrome.

4. Increased excretion of Calcium:

- Renal tubular disorders.
- Renal failure.

II. ALKALOSIS

- Total Calcium is kept constant BUT ionized fraction is decreased leading to Tetany.

1. Metabolic alkalosis.
2. Respiratory alkalosis.

Refer to "Nephrology"

استرجع كتابه

III. HYPOMAGNESEMIA

"Rare"

- Magnesium deficiency causes increased neuromuscular excitability → Tetany.

1. Malabsorption syndrome.
2. Diuretics: thiazides & furosemide.
3. CRF. ↓ reabsorption of Mg
4. Diminished intake: e.g. malnutrition.

CLINICAL PICTURE

I. LATENT TETANY

- Manifestations of tetany are not present.
- Manifestations appear by PROVOCATIVE TESTS.

1. Chvostek test:

- Tapping of the facial nerve in front of the ear → contraction of the facial muscles.

2. Trousseau's sign:

- Inflating the sphygmomanometer above SBP for 3 minutes → carpal spasm.

3. Erb's sign:

- Stimulation of nerves by less than 4 milli-amperes → muscle contraction, (normally: 8 milli-amperes at least are needed for stimulation).

II. MANIFEST TETANY

- Manifestations of tetany are present.

1. Irritability & parasthesia.

2. Muscle twitches & may be convulsions in severe cases.

3. Carpo-pedal spasm: spasmodic attacks affecting the carpal & pedal muscles.

4. Spasm of other muscles:

- Eye lids → Blepharospasm.
- Laryngeal muscles → laryngismus stridulus. (stridor)
- Facial & masseter muscles → risus sardonicus & trismus.
- Diaphragm → hiccough.
- GIT → abdominal colics.

5. Ectodermal changes: (Only in Hypocalcemia)

- Skin: atrophic, rough, falling of hair.
- Nails: brittle.
- Teeth: hypoplastic. loosening (also DM)
- Eye: cataract.

INVESTIGATIONS

1. In Hypoparathyroidism:

- Decreased serum Calcium, Decreased serum PTH, Increased serum Phosphate.

2. In Alkalosis:

- Normal serum Calcium, Normal serum PTH, Normal serum Phosphate.
- Decreased serum ionized Calcium.
- Increased pH.

3. In Hypomagnesaemia:

- Decreased serum Magnesium.

V. slowly
A. myophyl.
B. stimulant
Ca
Digitalis

TREATMENT

A) Treatment of the attack:

oral

also in the

- anaphylaxis
- tetany
- Hyperkalemia

to antagonize effect of K on Heart

- IV Ca gluconate: 10 ml of 10% solution over 10 minutes (very slowly) IV).

Cardiac arrest at systole

B) Treatment in between the attacks:

1. In Hypocalcemia:

- Ca gluconate: 1 - 3 mg / day orally.
- Vitamin D (cholecalciferol): 50,000 U / day orally.
- A T 10 (Dihydroxycholesterol): 0.5 mg / day orally.
- It increases Ca absorption from the intestine & phosphate excretion in urine.

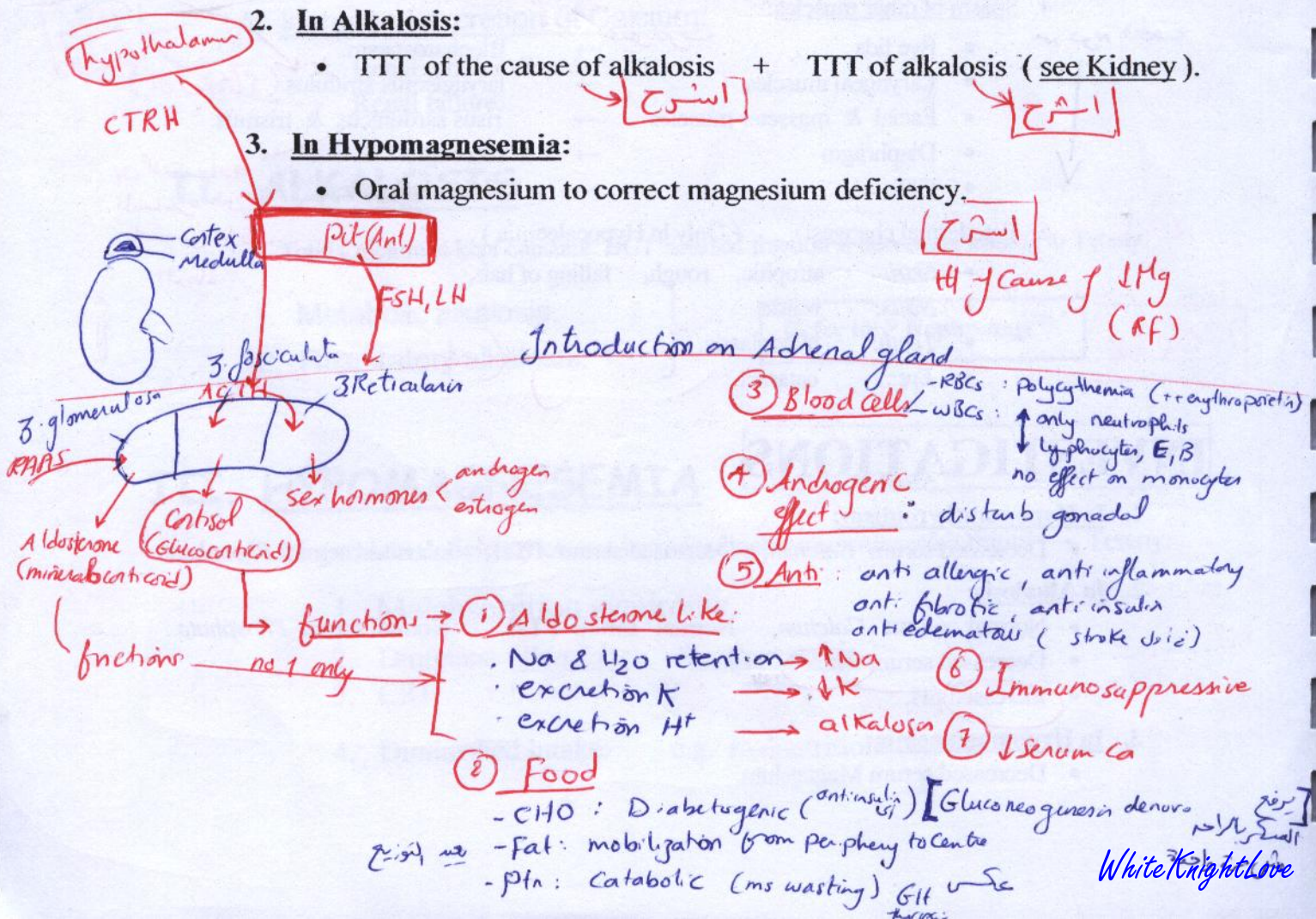
antitetic

2. In Alkalosis:

- TTT of the cause of alkalosis + TTT of alkalosis (see Kidney).

3. In Hypomagnesemia:

- Oral magnesium to correct magnesium deficiency.



CUSHING'S SYNDROME

Q Diagnostic evaluation

DEFINITION

- It is a clinical state resulting from: INCREASED GLUCOCORTICOIDS.

ETIOLOGY

A. IATROGENIC

لا يتم
مستور
وسين
منه انما

1. Prolonged administration of corticosteroids (Cushingoid syndrome):
2. Prolonged administration of ACTH (Cushingoid syndrome):

ما يكون سبب دوامه برا يعني اسه
Cushingoid

"The most common cause"

Exogenous cortisol
adrenalin rule of
B.A.

common.
less common - as multiple sclerosis

B. SPONTANEOUS

"The rare cause"

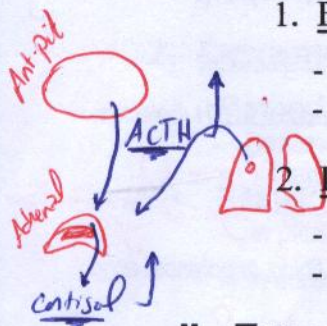
endogenous cortisol
مرحله بنج كورتيزول

I. Excess ACTH secretion:

1. Excess Pituitary ACTH secretion: = CUSHING'S DISEASE

- It occurs in pituitary tumours (pituitary adenoma).
- It represents 70 % of the spontaneous type.

not syndrome



2. Ectopic ACTH secretion:

- It occurs in paramalignant syndrome (e.g. bronchial carcinoma).
- It represents 15 % of the spontaneous type.

في ال حالات
cortisol ↑
(cushing)

II. Excess cortisol secretion:

- It occurs in primary adrenal tumours (e.g. adenoma or adenocarcinoma).
- It represents 15 % of the spontaneous type.

1. Adrenal tumor
ACTH ↓
by negative feed back

CLINICAL PICTURE

case clinical

- INCIDENCE: Age: 20 - 40 years, Sex: more common in females.

1. Disturbances in Fat metabolism:



- Moon-face: rounded face with bloated cheeks.
- Trunkal obesity: central obesity:
 - Increased fat in breasts & abdominal wall.
 - Hollow buttocks & thin limbs.
- Buffalo-hump: increased fat in the interscapular region.

fat → cells

Pit tumor & Lo! .
high ACTH
PMS & Lo! .
V.V. high ACTH
لانه في حاله
تفرز كورتيزول

2. PMS
e ACTH ↑
also MSH ↑ (pigment)
in pit tumor only
الوجه الداكن
hyper pigmentation

Lo! PMS
ACTH ↑
طاح كورتيزول

Oral
hyper pigmentation في Cushing
Pit. tumor
White Knight Love

fatal mistake - case curly :
in case Addison :
curly → polyuria
Addison → polyuria } different mechanisms

أولى تقول أبدأ في
anemic ← هشاشة
تبقى في الدم حاجة

حوار شفوي
أسباب
ery (drugs)

44

2. Disturbances in Protein metabolism:

- Muscles: wasting, weakness, myopathy.
- Bones: osteoporosis → backpain, kyphosis, pathological fractures.

Skin:

① Thin skin.

② Poor healing of wounds.

③ Vascular purpura:

④ Red striae (striae rubra):

⑤ stria alba: stretch

not calcium affection
but more: ptn affection

as spine is
weak (trabeculae & spongy)

due to ↓ collagen in B.V. wall (Catabolic on ptn)

Bruising due to ↓ support of the blood vessels. (↓ collagen) fragile

purplish lines on the trunk & thighs due to:

rupture of the weak SC collagen fibres → exposure of the vascular SC tissue.

⑥ ↑ skin infections (↓ immunity) Bact. fungal

3. Disturbances in Carbohydrate metabolism:

- Hyperglycemia & may be Secondary Diabetes (Steroid Diabetes).

4. Disturbances in Fluid & Electrolytes:

- Sodium: retention leading to hypertension.
- Potassium: loss leading to hypokalemia & polyuria (K diuresis).
- Alkalosis & tetany.

5. Other manifestations:

- Psychological symptoms: usually depression.
- Polycythemia: plethoric face. (+ + erythropoietin)
- Pigmentation of the skin: in cases of excess ACTH secretion, as MSH is part of ACTH molecule. (only) pituitary
- Infections: especially skin infections (fungal & bacterial). (imm ↓)
- Impaired growth: growth retardation occurs in children. catabolic effect against anabolism of G-H
- Impaired gonadal function: female: amenorrhea, hirsutism, acne, male: ↓ libido, impotence, acne.

Na ↑ sensitivity of B.V. wall to vasoconstrictors
volume ↑
Nephrogenic DI
↓ sensitivity of tubules to ADH

INVESTIGATIONS

I. Investigations to diagnose Cushing's syndrome:

1. Cortisol level in plasma:

- Normally: 5-20 ug % & there is normal circadian rhythm (lowest at midnight)
- In Cushing's: early: loss of circadian rhythm, late: persistent cortisol elevation.

2. Corticosteroid level in urine:

- Elevated urinary corticosteroids.

3. Blood chemistry:

- Increased Glucose, Increased Na, Decreased K.

4. Blood picture:

- RBCs: increased.
- WBCs: increased neutrophils, decreased lymphocytes, eosinophils, basophils.

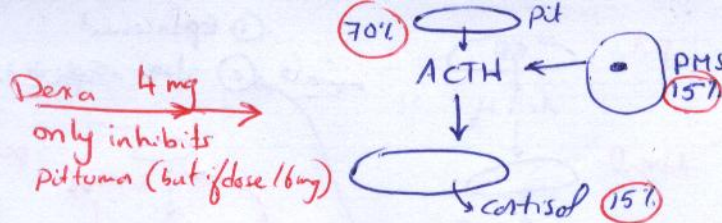
(highest at 8 am) 20

(lowest at midnight) 5

>20

أول مؤشر
هو تلك التي بالليل بدل
سبق 15 أو 20

Cortisol → ↓ Ca (by ↓ vit D)
↑ Ca (by bone resorption)



عمره ما يقل (Pit)
 يحل على
 عمره ما يقل (Pit)
 يقل بياغ pit tumor فقط لو ١٦ ملي
 45

5. Dexamethazone suppression test "low dose":

from Conn's disease of diagnosis

• Method:

- Dexamethazone (synthetic glucocorticoid) is given in a **low dose**: 0.5 mg / 6 h for 2 days.

(4 mg in total in the morning)

• Result:

- Normally:

cortisol level in the blood is suppressed, because: Dexamethazone will inhibit ACTH by -ve feedback.

- In Cushing's syndrome:

cortisol level in the blood is not suppressed, because: there is pathological secretion of either ACTH or cortisol.

لو بياقل cortisol

بقى مرتفع انه

بس ما عرفت ازاى نوع

لو قتل الكورتيزول يبقى
 exclude Cushing

6. Insulin-induced hypoglycemia:

- Normally:

it stimulates increase in plasma cortisol.

- In Cushing's syndrome:

no increase in plasma cortisol.

II. Investigations to diagnose the cause:

1. Plasma ACTH:

- **Low:** in primary adrenal tumours (due to inhibition of ACTH by -ve feedback).
- **High:** in pituitary tumours secreting excess ACTH.
- **Very high:** in ectopic tumours (as bronchial carcinoma) secreting much excess ACTH.

2. Dexamethazone suppression test "high dose":

• Method:

- Dexamethazone (synthetic glucocorticoid) is given in a **high dose**: 2 mg / 6 h for 2 days.

• Result:

- In pituitary tumour:

cortisol level in the blood is suppressed.

- In adrenal & ectopic tumours:

cortisol level in the blood is not suppressed.

لو ١٦ ملي

(+)

التفرقة clinically

بال pigmentary

3. Imaging:

a) Abdominal CT, MRI, or ultrasonography:

- To detect adrenal tumours.

b) Skull CT, MRI:

- To detect pituitary tumours.

c) Chest X-ray & CT:

- To detect bronchial carcinoma.

الحياة! ال عذبة pigmentary
 هو الحياة والى يبقى suppressed
 by high dose Dexa
 pit tumor هو عذبة

DIFFERENTIAL DIAGNOSIS

1. From other causes of obesity.
2. From other causes of hirsutism.
3. From other causes of hypertension. eg Hyperpara
4. From other causes of diabetes. eg Hemochromatosis
5. DD of the cause.
6. other causes of Polyuria eg: DM, DI, Hyperpara

TREATMENT

1. For adrenal tumours:

- Surgical removal of the tumour followed by suboptimal replacement therapy (low dose corticosteroids) for several months till the other atrophic gland recovers from suppression.

2. For pituitary tumours:

“ Cushing's disease ”

- Surgical removal or irradiation of the tumour, followed by replacement therapy.
- Nelson's syndrome: ttt of pituitary Cushing's disease by bilateral adrenalectomy may lead to the development of a locally invasive pituitary tumour with very high levels of ACTH & Hyperpigmentation.

3. For bronchial tumours:

“ Paramalignant syndrome ”

- TTT of the primary tumour, if possible.

surgery or chemotherapy

ADDISON'S DISEASE (CHRONIC ADRENAL FAILURE)

ETIOLOGY

I. PRIMARY ADRENAL FAILURE (Addison's disease)

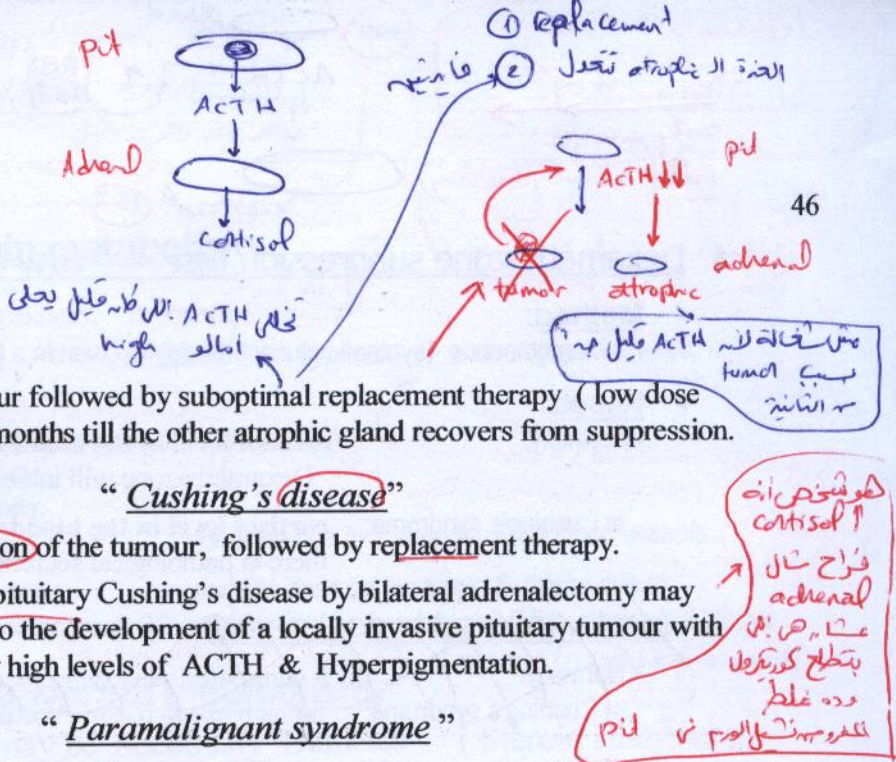
- Due to primary failure of the adrenal glands:

- **I**mmune: Autoimmune disease is the most common cause (80 %).
- **I**nfection: TB, HIV, Fungal.
- **B**ilateral: adrenalectomy.
- **B**ilateral: adrenal hemorrhage or infarction.
- **M**alignancy: Metastases especially from bronchial carcinoma, Lymphoma.
- **M**etabolic: Amyloidosis, Hemochromatosis.
- **C**ongenital: Hypoplasia & Hyporesponsiveness to ACTH.

II. SECONDARY ADRENAL FAILURE

- Due to secondary failure of the adrenal glands:

- Hypothalamic or pituitary disease, causing decreased ACTH level.



scheme for Cushing

المنهج
الكليني

CIP:

trunkal Obesity (fat), Osteoporosis (ptn), DM^{2ry} (CHO), HTN^{2ry} (electrolyte), Hirsutism, amenorrhea (others)



Investig.

cortisol (plasma, urine), DST (low dose)

do DST (high dose)

suppressible

not suppressible

70%

Pit Cushing (Cushing disease)

CIP: hyperpigmentation

Confirm

lab: ↑ACTH
Imaging: Brain CT & MRI

15%

Adrenal

low

Confirm

Imaging: abdomen

15%

Ectopic (PMS)

ACTH ↑↑↑ high

Confirm

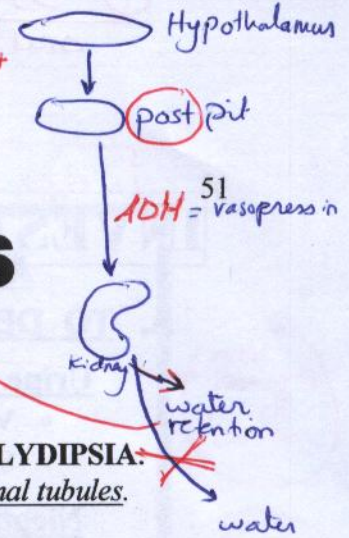
Imaging: chest

H/O Jatrogenic

White Knight Love

لا يفرغ الكلى زائداً على حاجته
stimulation
Hypothalamus
B.v. ينقل
فيحافظ على الضغط العالي
hypertension
يصطليح الـ

hypothalamus تنبأ بـ B.v.
Osmoreceptors
osmotic pr. $\uparrow\uparrow$
(Na $\uparrow$)



DIABETES INSIPIDUS

DEFINITION

- It is a clinical state of: **POLYURIA**, **NOCTURIA** & compensatory **POLYDIPSIA**.
- It is due to: deficiency of ADH, or lack of response to its action by the renal tubules.

ETIOLOGY

I. PITUITARY "CRANIAL" DI

"Deficiency of ADH"

- There is deficiency of ADH due to: damage of hypothalamus, posterior pituitary or hypothalamohypophyseal tract:

- **Idiopathic:** The most common cause.
- **Intracranial tumours:** primary or secondary or pituitary tumours.
- **Infections:** TB, meningitis.
- **Infiltrations:** Sarcoidosis.
- **Injury:** Head surgery (to the pituitary), Head trauma.
- **Irradiation:** Post-radiotherapy (to the pituitary).

II. NEPHROGENIC DI

"Defect in the renal tubules"

- There is lack of response of the renal tubules to the action of ADH:

- Hereditary.
- Acquired: hypercalcemia, hypokalemia, drugs as Lithium.

III. FAMILIAL DI

"Defect in the osmoreceptors"

- There is a hereditary defect in the osmoreceptors making them insensitive to changes in the osmotic pressure of plasma.
- This type is also called: essential hypernatremia.

CLINICAL PICTURE

1. Polyuria: marked **polyuria** by day & night (3-15 litres/day) & compensatory **polydipsia**.
2. **Dehydration**: & may be hypovolemic shock & may be ARF.
3. Complications of hypernatremia: hypertonic encephalopathy* (lethargy & coma).
4. Features of the cause: e.g. pressure manifestations of a tumour.

Na $\uparrow$ in ECF $\rightarrow$ water gets out of cells

Brain cells shrinkage

brain tumour

White Knight Love

N: 1-1.5 Litre

الإنسولين، الجلوكوز، $\text{ADH} \uparrow$ ، والدورة تغفل

Low fired sp gl. $\rightarrow$ also in R.F.
تفیر آخ

if possible. eg: removal of pit tumor

White Knight Love

DIFFERENTIAL DIAGNOSIS OF POLYURIA

* Polyuria = ↑ urine vol. > normal (N: 1-1.5 L)

I. Renal causes:

- Chronic renal failure.
- Polyuric phase of acute renal failure.
- Nephrogenic DI.
- Renal tubular disease.

most common renal cause

II. Endocrinal causes:

- Diabetes insipidus.
- Diabetes mellitus.
- Hyperparathyroidism & Hypercalcemia.
- Cushing's syndrome, Addison's disease & Conn's syndrome.

osmotic diuresis

most common endocrinal cause

III. Functional causes:

- Exposure to cold weather.
- Excessive intake of: fluids, coffee, tea.

IV. Hysterical polydipsia:

- Water deprivation test.

Q: Causes of polyuria: as cause of ARF

HIRSUTISM

DEFINITION

- Excessive growth of body hair in females.

ETIOLOGY

A. HIRSUTISM WITHOUT VIRILIZATION:

1. Idiopathic: the most common cause.
2. Iatrogenic: minoxidil, androgens, cyclosporin.
3. Familial & Racial.
4. Polycystic ovary: mild cases.

B. HIRSUTISM WITH VIRILIZATION:

1. Congenital adrenal hyperplasia.
2. Adrenal tumours.
3. Ovarian tumours.
4. Polycystic ovary: severe cases.

أمة ليس يهملها الله فهو معقود على كل الحاشي
بيت يموت الفار خلف جداره جوماً وبيت بالموائد مخف
تأكل لذل وتستفسر، لظماً وتنادي لا أريد إلا السلامة
فما نفعت أحاً وما دفعت غنياً وما رفعت راح

54

GYNECOMASTIA

حفظ
للاضوي
8 clinical

DEFINITION

- Enlargement of the male breast due to hypertrophy of the glandular tissue.

ETIOLOGY

"Decreased androgen / estrogen ratio"

1. Physiological:

- Neonatal ($\uparrow$ estrogen), pubertal ($\uparrow$ estrogen), old age ($\downarrow$ androgen).

2. Pathological:

a) Endocrinal: Hypogonadism, Hypothyroidism, Hypothyroidism.
b) Metabolic: Chronic renal failure, Liver cell failure.
c) Malignant: Estrogen-producing tumours of the testis or adrenals.

failure.
spironolactone (ascites)
Cimetidine (gastitis)

3. Iatrogenic:

- Estrogen,

Digitalis,

Spironolactone,

Cimetidine.

H₂ receptor blockers

4. Idiopathic.

HYPOGLYCEMIA

ETIOLOGY

1. Endocrinal:

- Hypopituitarism. Simmond's, Sheehan
- Addison's disease.
- Hyperinsulinemia: overdose of insulin, insulinoma, paramalignant, CRF.
- Myxedema Coma

2. Non - Endocrinal:

- Decreased glucose intake: starvation.
- Decreased glucose absorption: malabsorption.
- Increased demand: heavy exercise & pregnancy.
- Increased loss: renal glycosuria.
- ACUTE LIVER FAILURE.

CLINICAL PICTURE

1. Insufficient glucose to the brain leading to:

- Lack of concentration, mental dullness, hallucinations, tremors, convulsions, coma.

2. Manifestations of sympathetic overactivity due to hyperadrenalism:

- Irritability, tremors, pallor, sweating, palpitation (tachycardia).

VC

INVESTIGATIONS

1. Blood: markedly low blood glucose (less than 50 mg / dL).
2. Urine: no glucose in urine.

3. Investigations for the cause.

eg. insulinoma

except renal glycosuria

DKA: glucose = urine

N: 70 - 110 mg/dl
fasting
لا نريد
110

TREATMENT

1. TTT of the cause.
2. TTT of hypoglycemic coma: "refer to DM".

eg: insulinoma: surgical removal

شرح

OBESITY

SQ: complications of obesity
[oral]

DEFINITION

- A state of excess ADIPOSE tissue mass.

ETIOLOGY

I. IDIOPATHIC (95 %)

1. Familial: genetically determined factors or same pattern of eating.
2. Excessive caloric intake: excessive intake of fats or carbohydrates.
3. Diminished caloric consumption: physical inactivity.

عادات تأكل كثير

ناكل أكثر من حاجته فيتم تخزين
adipose

II. SECONDARY

1. Endocrinal: Cushing's syndrome, Myxoedema, Hypogonadism, Insulinoma, Pregnancy.
2. Hypothalamic disturbances: Diabetes insipidus, polyphagia, obesity, hypersomnia.
3. Drugs: they stimulate the appetite, e.g. insulin, CCPs, corticosteroids.

↑ lipogenesis
↓ lipolysis
stimulate appetite

MEASUREMENT

1. **Body Mass Index (BMI)** = $\frac{\text{Weight}}{\text{Height}^2}$ (Average: 18 - 25).
Mild (BMI = 27 - 30), Moderate (BMI = 30 - 40), Marked (BMI > 40).
2. **Anthropometry**: measure the skin fold thickness, e.g. over the Triceps.

25 - 27
over wt
سليم
Sunderant

DISTRIBUTION OF BODY FAT

- Measure the: WAIST / HIP ratio:

1. Male (Android) pattern:

- More fat in the upper body (associated with more morbidity & mortality).

Abdominal
Apple



2. Female (gynecoid) pattern:

- More fat in the lower body (associated with less morbidity & mortality).

pelvic
pear



COMPLICATIONS

1. METABOLIC SYNDROME:

- Refer to "DM".

syndrome X

2. CARDIOVASCULAR:

- Coronary artery disease.
- Hypertension.
- Hyperlipidemia & Atherosclerosis.
- DVT & Varicose veins.

(risk factors of obesity
on coronary)

- 1- Physical inactivity (for collateral)
- 2- Diet rich in saturated fat
- 3- Hyperlipidemia

3. RESPIRATORY:

- Restrictive hypoventilation & Pickwickian syndrome.
- Sleep apnea syndrome. & intermittent cessation of breathing during sleep

1
2
3
4

marked obesity > 40 kg/m²
Secondary Polycythemia (severe hypoxia)
Hypocapnia
Bony from somnolence (Coccarosis)

Flappy vessels walls

4. GIT:

- Cholesterol gall stones & cholecystitis.
- GORD & Hiatus hernia.
- Fatty liver.

as fat
→ Restrictive
hyperventilation
↓
Weakness
apnea
↓
+ CO₂, O₂ ↓, pH ↓

5. NEUROLOGICAL:

- Cerebrovascular Stroke.
- Carpal tunnel syndrome. entrapment

6. JOINTS:

- Osteoarthritis. esp. knee → hip → lower spine
- Back pain.
- Increased incidence of gout.

degenerated cartilage by wt ↑

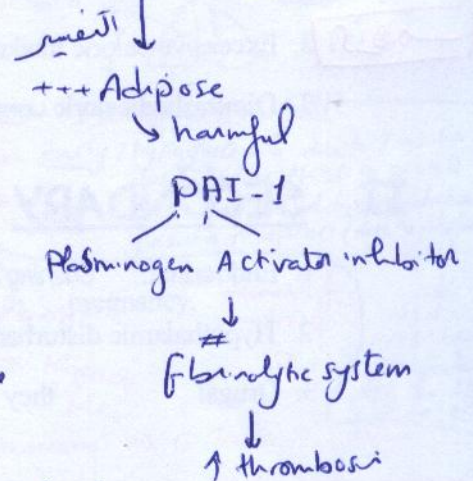
↑ intake of purines
2 Insulin resistance → ↑ U.A.
↑ uric acid

7. MALIGNANCY:

- Increased incidence of: cancer colon, rectum, GB, breast.

8. PSYCHOLOGICAL:

- Depression, Anxiety.



Weakness
apnea
↓
+ CO₂, O₂ ↓, pH ↓
↓
potent stimulus for RC (intermittent)

TREATMENT

1. Reduction in caloric intake:

"Diet ttt"

- The aim is to lose 1 kg / week.

2. Increase in caloric loss:

"Exercise"

- It should be encouraged, BUT: *exercise alone is not enough to lose weight.*

3. Drugs:

a) Anorexic drugs:

e.g. fenfluramine.

b) Oleristat:

inhibits the pancreatic lipase & so decrease fat absorption.

~ Diet

↓ appetite

or (Biguanides) for diabetic

malabsorption

4. Surgery:

a) Jejunio-ileal bypass:

causes malabsorption (not used now) X

b) Gastric balloon:

a balloon is placed endoscopically in the stomach & inflated.

c) Gastric plication:

stapling across the stomach will produce a small gastric pouch.

OSTEOPOROSIS

DEFINITION

Reduction in the BONE MASS leading to:

- Increased bone fragility.
- Increased risk of fracture. *esp trabecular spine neck femur*

ETIOLOGY

1. POST-MENOPAUSAL (Type I). → $\downarrow$ Estrogen } needed for good osteoblastic activity
2. OLD AGE men (Type II). → $\downarrow$ Androgen }
3. Endocrinal: Cushing's syndrome, Hypogonadism, Hyperthyroidism, Hyperparathyroidism. *Ca*
4. Failure: Renal failure, Liver failure, failure of absorption (MALABSORPTION). *turn over $\downarrow$ $\uparrow$ Ca - Blood*
5. Malignancy: Multiple myeloma, terminal malignancy, osteolytic metastasis. *vit D*
6. Iatrogenic: Corticosteroids, long term heparin, long term diuretics.
7. Inherited: Osteogenesis imperfecta.
8. Immobilization. *bone wasting*
9. Idiopathic.

CLINICAL PICTURE

1. EARLY:

- Asymptomatic.

2. LATE:

- Bone pains & Bone tenderness.
- Pathological fractures & Deformities.

esp spine: Kyphosis

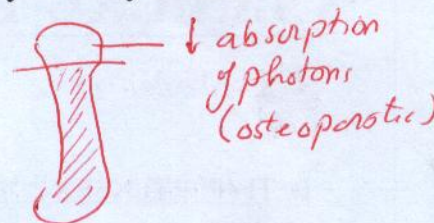
INVESTIGATIONS

1. Plain X-ray:

- Decreased bone density (osteopenia).
- Deformities, fractures, vertebral collapse.

2. Bone Densimetry:

- Measure the bone mass by: Dual Energy X-ray Absorptiometry "DEXA".
- It measures: the absorpti on of a beam of photons generated by an X-ray source to determine the BONE DENSITY.



TREATMENT

1. GENERAL MEASURES:

- Diet: adequate Proteins, Calcium, Vitamin D.
- Calcium carbonate orally.
- Vitamin D orally.

2. HORMONE REPLACEMENT THERAPY (HRT):

- Estrogen therapy: especially in premature menopause, ovariectomy, hypogonadism.
- Androgen therapy: should be given to hypogonadal men.

3. BIPHOSPHONATES:

- They inhibit bone resorption.

also chelate
- ↑ Ca = blood

4. CALCITONIN.

- inhibit bone resorption

Nasal spray

(Miacalcin)

5. TTT of the cause:

e.g. Cushing's syndrome.

PHEOCHROMOCYTOMA سيفو

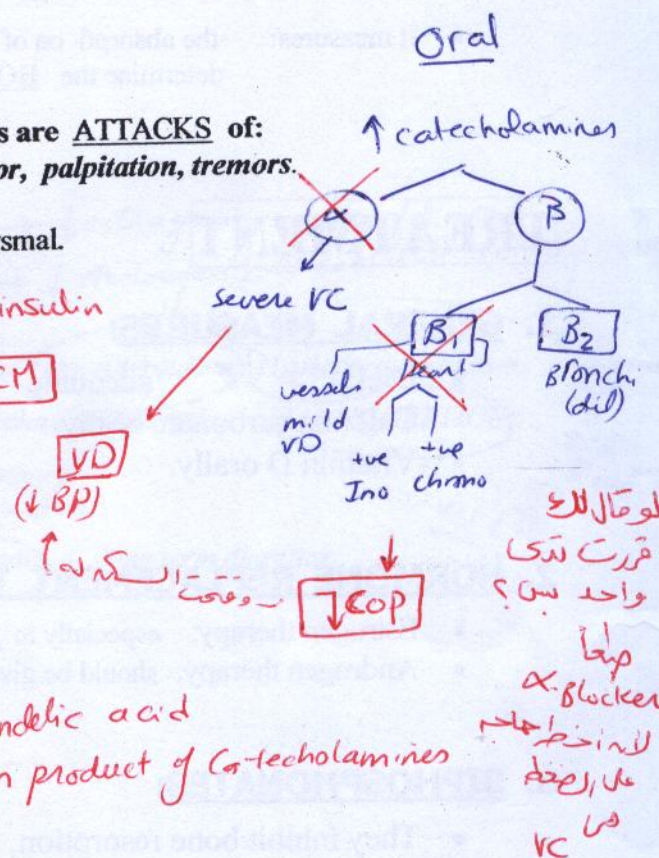
DEFINITION

- Tumours that secrete CATECHOLAMINES.
- 90 % arise in the ADRENAL MEDULLA, others in the sympathetic chain in abdomen.
- 90 % are UNILATERAL.
- 90 % are BENIGN.

Adrenaline, Nor Adrenaline, $\pm$ dopamine
(pulsatile in paroxysms)

CLINICAL PICTURE

1. GENERAL: the commonest symptoms are ATTACKS of: headache, sweating, pallor, palpitation, tremors.
2. HYPERTENSION: secondary & paroxysmal.
3. DIABETES: secondary. as anti insulin
4. HYPERTROPHIC CARDIOMYOPATHY. HCM



INVESTIGATIONS

1. INCREASED CATECHOLAMINES:
- In plasma & in urine.
2. INCREASED URINARY VMA.
3. IMAGING:

- CT, MRI: of the abdomen.

- **MIBG**: scanning with **M**eta **I**odo **B**enzyl **G**uanidine produces specific uptake in sites of sympathetic activity.

detect overactivity
Localize site of overactivity

TREATMENT

1. Surgical: removal of the tumour is the ttt of choice if possible.
2. Medical: combined alpha & Beta adrenergic blockers:
 - For pre- & post- operative ttt.
 - If surgery is not possible.

introduction to DM

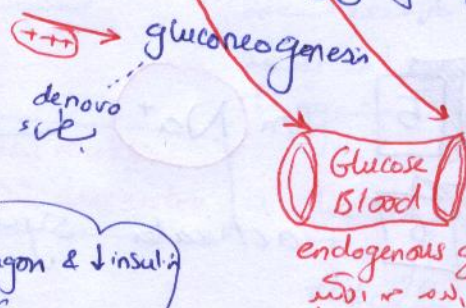
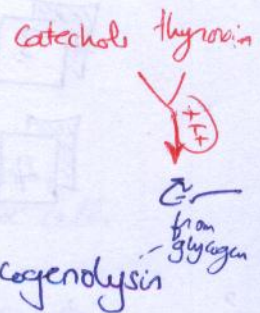
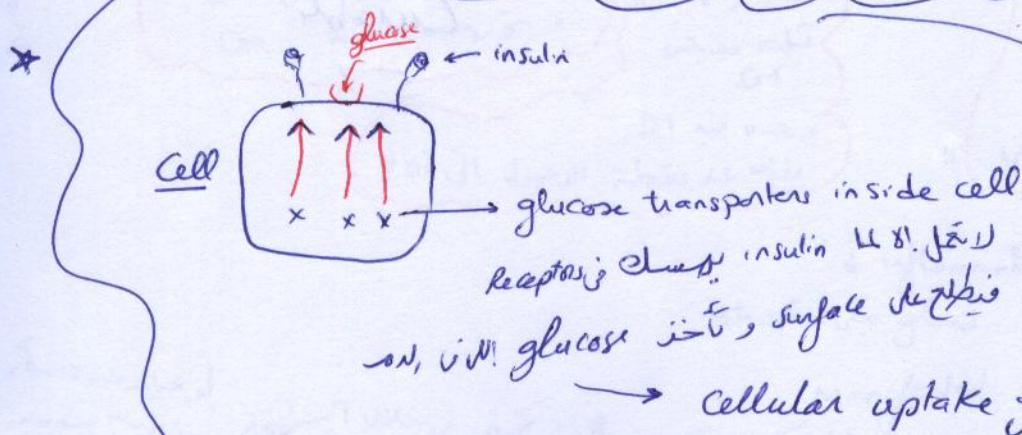
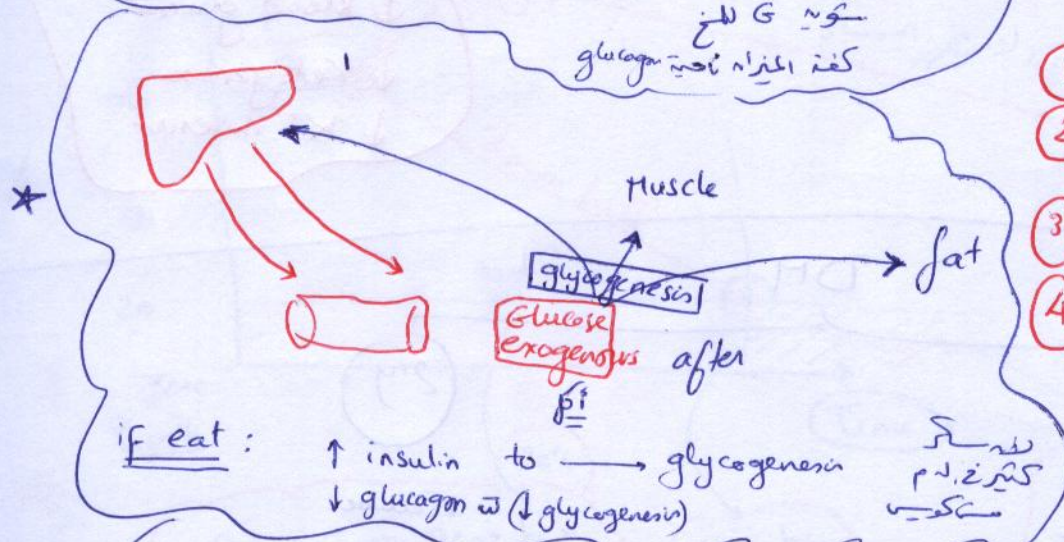
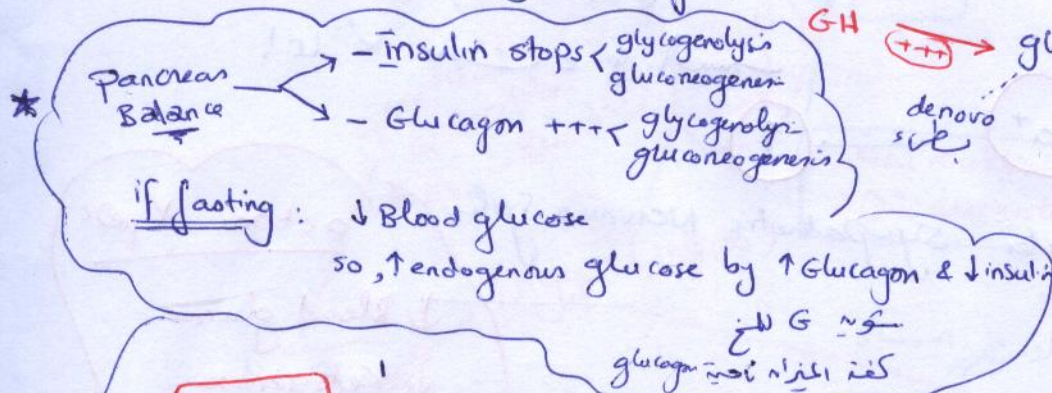
hormones

↓ glucose
insulin

↑ glucose
G.H.
Glucagon
Catecholamine
Cortisol
Thyroxine

Insulin

1. polypeptide : multiple a.a.
2. from : pancreas (islet cells $\Rightarrow$ B cells)
3. Receptors : liver, fat, Ms
4. Main action : * lowering down of Blood Glucose



- 1 ↓ glycogenolysis
- 2 ↓ gluconeogenesis
- 3 ↑ glycogenesis
- 4 ++ Glucose transporters

فتوصيه في الدم
وتنتفع به الخلية

WhiteKnightLove

1] ↓ Blood glucose

5. other actions

2]

* ↑ Lipogenesis
↓ lipolysis

pt e insulinoma → خفي
pt e IDDM → خالص

* ↓ Ketogenesis

ورده يحتاج
نقطة واحدة
insulin

v. small insulin is
enough to prevent
Keto acidosis

لذلك الحارة الى معسر

insulin
cell

Ketoacidosis هو الـ بيلة

3]

v. mild anabolic (onptn)

4]

on K^+ of body NO Effect

as it shifts it from serum to inside cell
(↓ serum K) *

ك⁺ ثابت في الجسم

5]

on Na^+

→ ↑

6]

activates Sympathetic Nervous system

actions يوتي

↓ Blood glucose

↓ Ketogenesis

↓ K^+ in serum

DM

1y

no Cause
Controllable

95 %

2y

Cause
Curable

5 %

(Cockback 2)
- pericarditis
- pleurisy
- aseptic meningitis
- DM

Complication
GRF
coma emergency
(Clinical) short or long
CRP's
Case
oral 1000

14

DIABETES MELLITUS

DEFINITION

- A chronic disorder characterized by impaired glucose metabolism → **HYPERGLYCEMIA.**
- It is associated with secondary changes in multiple organs → **COMPLICATIONS.**
- It is due to: **Insulin deficiency** (I) **Insulin resistance** (II) OR Both.
- **INCIDENCE:** It is the most common endocrine disease, 1-2% in most of the communities.

ETIOLOGY & PATHOGENESIS

1. PRIMARY DIABETES

TYPE I Insulin Dependent Diabetes Mellitus (IDDM)

- It is also described as:
- It was previously termed:
- It essentially depends on:

• Predisposing factors:

1. Genetic factors:

- There is association with certain HLA types. - over expressed in this p.t.
- There is 50 % incidence in identical twins.
- There is ↑ risk of inheritance: **30% if both parents are diabetic.**

2. Immunological factors:

- Immunologic markers: Islet Cell Abs (ICAs) & Anti-insulin Abs.
- **INSULITIS:** Infiltration of pancreatic islets with **LYMPHOCYTES.**
- Associated AI diseases: e.g. **Coeliac dis, Grave's dis, Addison's dis.**

TYPE I DM is further divided into 2 subtypes:

- Type I A: Immune-mediated β cell destruction with **presence** of Immunologic markers.
- Type I B: Idiopathic β cell destruction with **absence** of Immunologic markers.

3. Environmental factors:

- They trigger the autoimmune process: in the genetically susceptible individuals.
- The most important factors are: Viral infection (**Coxsackie & Rubella**).
CMV mumps

• Insulin abnormality:

- **INSULIN DEFICIENCY:** secondary to destruction of the β - cells.

>95%

very rare <5%

میزان القیم
هو الوقایة
لوطیل زبانه DM
نسبتة 30% اغلایه
دله screening
لازم موجوده نه بدری

لوقتیمر → IA → اغلایه → immunosuppressant → فلاسین
موجوده

WhiteKnightLove

Type 1

Genetic

HLA = Human leukocyte Ag
= MHC = Major Histocompatibility Complex

genes

on chromosome 6

overexpressed

eg: DR₃ DR₄
DQ₂ DQ₈



oral

destruction of B cells

is selective

B cells only
& sparing α cells

slow

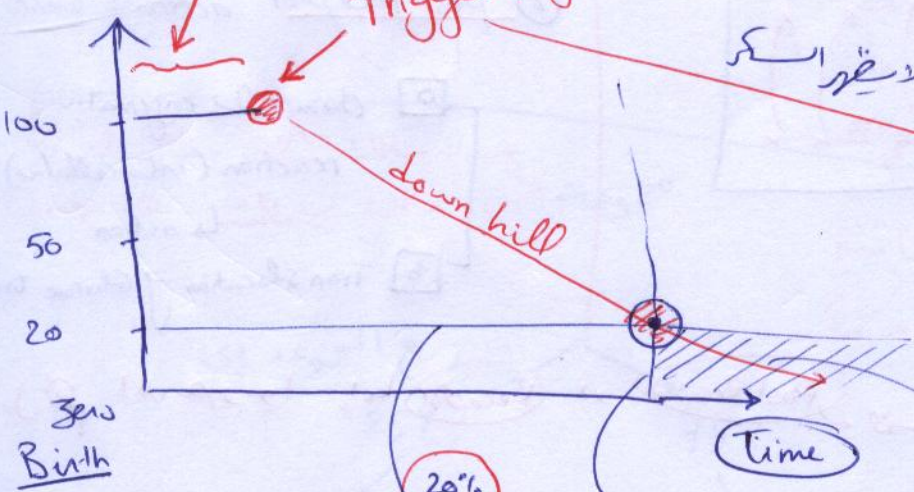
triggering (infection)

when reaches 80% destruction

becomes manifested clinically

genetically susceptible
& Abs in Blood

Trigger (infect)



DM

DM

DM

↓ inflammation
atrophic gland

manifested

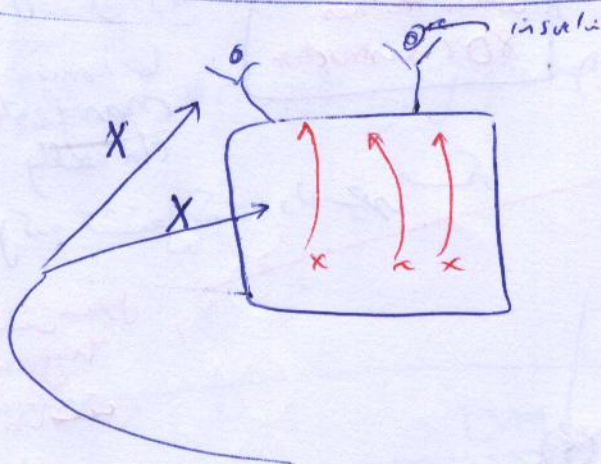
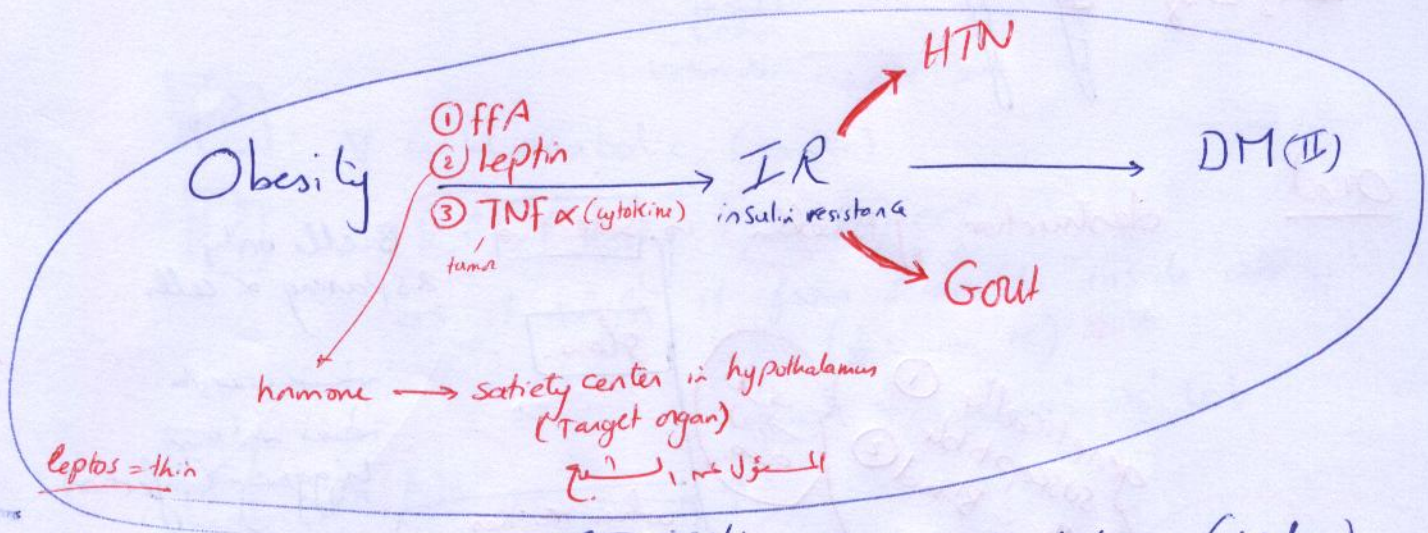
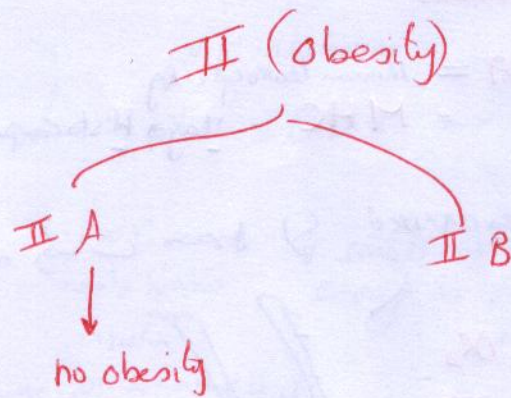
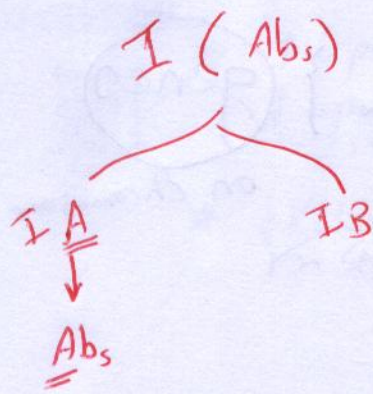
Ab

White Knight Love

DM

DM

DM



① Receptor Action (binding)

② post receptor action

- a chemical & enzymatic reaction (intracellular) → action
- b Translocation of Glucose transporter

٣ دمل ٢م! لا-حرجوا، لا (Receptor) و (Post Receptor) ٢م

لكن هذا الحياه من هيفضل محبى
DKA
لكن متأخر جبات المرض
يوقى بالانضبط زي (I)
لما في ملاكك بتوظم

وهو عنده Insulin resistance
لكن ده من معناه انه ineffective
100%
لكن فيه نوع effect
من كافي انه يمنع كى
لكن كافرا انه يمنع غيبوبة سكر

TYPE II Non - Insulin Dependent Diabetes Mellitus (NIDDM)

- It is also described as: "Ketoacidosis resistant".
- It was previously termed: "Maturity-onset diabetes".
- It does not essentially depend on: INSULIN in its treatment.

• Predisposing factors:

1. Genetic factors:

- There is ~~no~~ association with certain HLA types.
- There is 100 % incidence in identical twins.
- There is ↑ risk of inheritance: 40 % if both parents are diabetic.

2. Obesity:

- It is absent in: 20 % of the patients
- It is present in: 80 % of the patients
- INSULIN RESISTANCE: due to secretion of

Pathogen
العدوى الميكروبية

autoimmune
autoimmune
تبقى من ماله حاجه

Risk factors of ID

1. Age > 45 y. old
2. Family H/O
3. Obesity > 27 Kg/m² (JP)
4. Gestational DM H/O
5. IFG IGT
6. HTN (IR) > 140/90

(Type II A).

(Type II B).

Leptin & FFAs.

TNF-α

impaired fasting glucose

impaired Glucose tolerance

• Insulin abnormality:

الصفحة القادمة

❖ INSULIN RESISTANCE: "IR"

- Decreased insulin action on target tissues (muscle & liver) due to:

- Receptor defect: ↓ insulin receptors in target tissues (Minor role).
- Postreceptor defect: in target tissues (Major role).

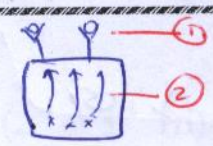
❖ IMPAIRED INSULIN SECRETION:

• Initially:

- ↑ insulin secretion occurs due to IR to maintain normal glucose

• Later:

- ↓ insulin secretion occurs due to islet cell failure secondary to "Glucose toxicity".



Persistent
"Hyperinsulinemia".
Hyperglycemia

❖ INCREASED HEPATIC GLUCOSE PRODUCTION:

- IR → failure of insulin to suppress gluconeogenesis → Fasting hyperglycemia.

* Sulphonylureas → تحسين السكر ٣ حاجات دول

↓ insulin
↓ lipogenesis ↑ lipolysis

	Type 1	Type 2
Incidence	10 %	90 %
Age of onset	Less than 30	More than 30
Body weight	Usually decreased	Usually increased
Severity	More severe	Less severe
Complications	More common	Less common
Coma	DKA	Hyperosmolar coma
Insulin level	Low or absent	High (early), low (later)
Insulin therapy	Always essential	Not always essential
Oral hypoglycemic drugs	Not effective	Effective

SPECIAL TYPES

Maturity Onset Diabetes of the Young (**MODY**)

A subtype of type 2 diabetes, but the main defect is impaired insulin secretion & not IR. not glucose toxicity

• **Etiology:**

GENETIC defects in insulin secretion:

(6 variants: MODY 1, **2**, 3, 4, 5, 6 due to mutations in 6 genes).

• **Onset:**

YOUNG, Early onset of Hyperglycemia:

(Between: 10 – 25 years).

Latent Autoimmune Diabetes of the Adult (**LADA**)

A subtype of type 1 diabetes, but autoimmune β – cell destruction is slow.

• **Etiology:**

AUTOIMMUNE β – cell destruction.

• **Onset:**

ADULT, Late onset of Hyperglycemia:

(Above: 30 years).

BRITTLE DIABETES

- A type of diabetes with wide unpredictable fluctuations in blood glucose levels.
- Also called: unstable diabetes or labile diabetes.

قصة عليه مكتبة له ريشة وظيف له diet راج و جالك رجاك مضبوط يبقى تمام
لو جالك من مضبوط اما انه انكاه او الدوام مضبوط
او الككل و الدوام مضبوط ام فيه مشكلة عنه ←

WhiteKnightLove

2. SECONDARY DIABETES

- Cause
- Curable
- (< 5 % of DM)

1. Pancreatic exocrine diseases:

- Chronic pancreatitis, Cancer pancreas, Cystic fibrosis. *malabsorp*
- Hemochromatosis, Pancreatectomy. *in Cancer Insulinoma*

2. Endocrinal diseases: "Increased Anti - insulin hormones"

- Increased GH: *Acromegaly.*
- Increased Glucagon: *Glucagonoma.*
- Increased Catecholamines: *Pheochromocytoma.*
- Increased Cortisol: *Cushing's syndrome.*
- Increased Thyroxin: *Thyrotoxicosis.*

*2ry HTN
Glucagon*

3. Renal diseases:

Chronic renal failure. → late (down regulation of Insulin)

4. Liver disease:

Chronic liver failure. → IGT

5. Drugs:

- Corticosteroids, Thyroid hormone.
- Diazoxide, Diuretics (*Thiazides, Frusemide*).

+ Hyperuricemia

6. GESTATIONAL DM:

- IGT: first detected during LATE PREGNANCY (2nd or 3rd Tri).
- Etiology: ① IR + ② ↑ secretion of Anti - insulin hormones in late preg. *from placenta*
- Incidence: 2 % of pregnant women.

• COURSE:

- Usually: *reverts to normal after delivery.*
- In 40 %: *passes to Type 2 diabetes within 5 - 10 years.*

CLINICAL PRESENTATIONS

1. Asymptomatic: *Accidentally discovered.*
2. Symptomatic: **5 P**
 - **P**olyuria, **P**olydipsia, **P**olyphagia, **P**ruritus, **P**arasthesia.
 - Loss of weight: *in type 1 diabetes. ↓ insulin*
3. Complications: affecting multiple organs **or** acute complications (coma).
4. Cause: in case of secondary diabetes.

*eg: CRF
Hemochromatosis*

Oral

حوار

Q اوصف مظاهر 1 و 2 و 3 و 4

A: ② ↑ → ↓ / ① ↓

Q: ايه اللى كسر B cell في 1 و 2

A: ① by Abs (1/2) predisposit / ② by Glucose toxicity

Q: هو فيه toxicity على 3 و 4

A: ① toxicity of HbA1c

Investigation

Normal

DM

FBS
Sugar

not > 110 mg/dl

IFG

impaired fasting glucose
لا يفرط

> 126

بين لازم قرائنه

2hpp
جلوكوز

not > 140

IGT

200

75gm
جلوكوز

RBs

Random Blood sugar

> 200

بس لازم يكون

Symptomatic

fasting 115

سواء جالك متكرر

2hpp 150

مجموعة > او جالك مرة واحدة

← واحدة (واحدة) كافية

← في fasting لازم متكرر

ربع المجموعة دي

25%

75%

II

متكرر

متكرر
II

لذلك لازم تقول للعيا
follow up

DM is a laboratory diagnosis : مختبري
مختبري
diabetic

= fasting Blood glucose

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CRITERIA FOR DIAGNOSIS OF DM

1. FPG: ≥ 126 mg / dL on at least 2 separate occasions.
2. Two-hour PG: ≥ 200 mg / dL during an OGTT.
3. Symptomatic DM: plus RPG ≥ 200 mg / dL.

CRITERIA FOR DIAGNOSIS OF IFG & IGT

1. IFG: FPG is: 110 – 126 mg / dL on at least 2 separate occasions.
2. IGT: Two-hour PG is: 140 – 200 mg / dL during an OGTT.

- Both: represent a state of Hyperglycemia but do not meet the criteria for diagnosis of DM.
- Both: do not produce classic symptoms or complications of DM.
- Both: are at risk for developing Type 2 DM (25 %).

يُكتشف المرض يقول أحد ذلك أن من ضبط السكر في الدم خلال فترة ما قبل أو ما بعد الأكل يبقى هو مرضي يقول أحد أكبر طائفة الدم 120 يوم واحد طائفة الدم مرة Zero يوم

INVESTIGATIONS

1. Plasma glucose: "Fasting & 2 hours post prandial"

- Normal levels:

- FPG: 70 – 110 mg / dL
- Two-hour PG: less than 140 mg / dL

- Abnormal levels:

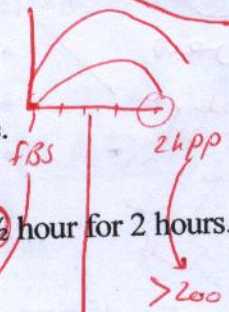
- Diagnosis of DM: see before.
- IFG & IGT: see before.

False normal of HbA1c
 ① H.A.
 ② attack hyperglycemia
 when plasma glucose is low

malabsorption
 Myxedema

2. Oral Glucose tolerance test (OGTT):

- Fasting blood & urine are collected & measured for glucose.
- The patient is given 75 gm glucose in 300 ml water orally.
- Blood & urine are collected & measured for glucose every 1/2 hour for 2 hours.



3. Urine analysis:

- To detect: glucose or acetone in urine.

4. Monitoring of treatment:

- Plasma glucose monitoring.

- Glycosylated hemoglobin (Hb-A1c):

- Formation: by linkage of glucose to β chains of Hemoglobin A.
- Value: $\frac{\text{glycated Hb}}{\text{total Hb}} \times 100$ estimates the efficiency of DIABETIC CONTROL during the preceding several weeks (6 – 12 weeks).
- Normal level: 6 % of the total hemoglobin. 15 gm average

Oral Pathways
 Urine
 Glucose acetone
 - - normal
 + -

- 1 uncontrolled DM
- 2 renal glycosuria
- 3 Hyper osmolar non ketotic

5. Investigations for:

Complications,

Cause (in secondary diabetes).

eg { CRF : RFT
 Acute MI : ECG

insulin → ↑ lipolysis → ↑ ketones
 ketones → White Knight Love

DKA = $\frac{T}{I} \frac{I}{I} \frac{I}{I}$

starvation ketosis

proper control : to delay complications but they will occur (inevitable)

الأكثر حاجة نظرياً
هو الـ ٣

COMPLICATIONS

اكتب مع Comas

I. CARDIOVASCULAR

3

1. Macrovascular complications:

"Macroangiopathy"
"Atherosclerosis"

- CAD: Angina, AMI (may be painless), HF, Sudden death. *most common cause is CAD*
- CVD: Stroke (cerebral thrombosis → hemiplegia).
- PAD: Ischemia of LL (intermittent claudications & gangrene). *most common cause of nontraumatic amputation of L.L.*

2. Microvascular complications:

"Microangiopathy"

- Neuropathy.
- Retinopathy. *earliest*
- Nephropathy. *latest*

والتشخيص في ١٢ سنة أو أكثر
لو جالك عنده nephro يبقى غالباً القاعده عنده متغيره عنده HTN
في تشخيصه عنده DM - يكون بـ IGT
(multiple metabolic abnormal) = اختلالا بسموها في

3. METABOLIC SYNDROME:

"Syndrome X"

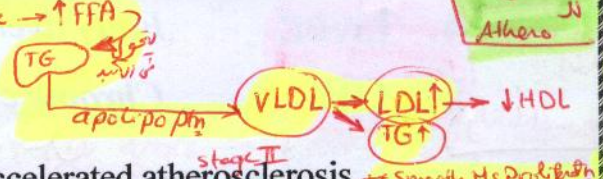
Case

- ③ • HYPERTENSION. (IR of obesity)
- ② • IR → HYPERGLYCEMIA (IFG or IGT or Diabetes). *only*
- ① • OBESITY, esp. abdominal *Android (distribution of fat)* *only in type II obese*
- ④ • Atherogenic DYSLIPIDEMIA (high TG, low HDL & high LDL). *late*

رصد → Definition of Athero:

ATHEROSCLEROSIS IN DIABETES

1. Dyslipidemia. *↑↑ adipose → ↑ FFA*
2. Endothelial dysfunction. (due to ↑G)
3. ↑ liability to HTN. (high risk)
4. ↑ Cytokines → ↑ growth factors → accelerated atherosclerosis. *stage II*
5. Prothrombotic state: ↑ fibrinogen, vWF, PAI-1 & ↑ platelet aggregation. *↑ rennin → RAAS*



تفسير
DM له high risk
له Athero

oral
الخطر
LDL
وال LDL
نوعه
large small
MW MW
↓
الخطر لانه
يسببه
تحت في
endothelial
pores
deposited
internal
wall
يرجع
plaques
عبارتي
pathology

GRF

HTN IN DIABETES

1. Endothelial dysfunction. (due to ↑G) [vascular growth]
2. Insulin resistance.
3. Diabetic nephropathy. *↑ rennin → RAAS*

platelet
clotting

Complications

DM $\rightarrow$ $\uparrow$ glucose $\rightarrow$ harmful ALL

- GEP $\leftarrow$ ① Advanced glycation end products
DAG $\leftarrow$ ② Diacyl glycerol DAG
S $\leftarrow$ ③ Sorbitol (intracellularly)
④ O_2 free radicals (oxidative stress)

Oral

(Antioxidants PO_4^{3-})
aspirin
↓ dose
min 81
Vitamin Hage

DM $\hat{=}$ $\uparrow$ incidence of infection

(GRF)

- ① hyperglycemia $\Rightarrow$ good medium of infection esp $\leftarrow$ Bacterial
fungal
- ② Impaired immunity $\Rightarrow$ due to ① $\downarrow$ phagocyte fn
② $\downarrow$ neutrophil chemotaxis
- ③ Ischemia : impaired blood supply

(مخالفت اقواله انعاله هارت افعاله)

COMA, stroke ← أخطر
PN ← أسوأ

20

II. NEUROLOGICAL

4E

1. Cerebral complications: "emergencies"

- * • COMA: of different types, "see later". استرجع كالمه
- * • CVD: Stroke (cerebral thrombosis → hemiplegia).
- INFECTIONS: fungal (rhinocerebral mucormycosis). nose في دماغ

also
aseptic
meningitis

2. Spinal cord complications: "rare"

- Posterior column affection: Sensory ataxia.
- Pyramidal tract affection: Diabetic lateral sclerosis.

Cavernous Sinus thrombosis

brain في nose
(fungal)
Cavernous Sinus thrombosis
Cavernous Sinus thrombosis

3. Root complications:

- Radiculitis: esp. affecting the roots of sciatic nerve (SCIATICA). 4, 5 5/33
- Posterior root: pain & parasthesia, then, sensory loss. late
- Anterior root: weakness & wasting. early

Cauda equina
cauda equina
lumbosacral

4. Peripheral neuropathy:

- Refer to "neurology". استرجع كالمه

DM most common cause of PN

no fasciculation
root 2 في AHCs

III. GIT

5E

↑TG → bacterial fermentation → lactic acid → demineralizes tooth enamel

1. Mouth: Dental caries, gingivitis, loosening of teeth. decay

2. Stomach: Gastroparesis + N, V & acute abdominal pain during DKA. GRF

3. Intestine: Diarrhoea. GRF

4. Liver: Fatty liver. as ↑TG input in liver

5. GB: Chronic cholecystitis & gall stones are common.

- 1. ↓ intest. motility (bact. overgrowth)
- 2. ↑ infection incidence (infective)
- 3. ± ↑ intest. motility

- ① inflammation of wall
- ② ↑ incidence of infection

- ① on top of inflammation (infection)
- ② ↑ cholesterol in blood
- ③ ↓ motility

IV. RESPIRATORY

1. INFECTIONS:

especially TB & Pneumonias.

2. During DKA:

(Breath problems)

- Rapid deep breathing (Kussmaul's breathing)
- Acetone odour in the breath. (K.B.)

Metabolic acidosis
DKA
RF

Unresolving
Pneumonia
أخذ الذا
أسرع ولا
أسرع ولا

Cholecystectomy
gall stone
DM
White Knight Love

V. GENITAL

1. Males:

Impotence.

→ autonomic neuropathy (parasymp.)
ولا أحب أدوية BB التي تزيد إفرازات
impotence

2. Females:

- Pruritus vulvae. (↑G)
- INFECTIONS: vaginal moniliasis.

DIABETES & PREGNANCY

I. Effects on DM on pregnancy:

On mother:

- Post-partum hemorrhage & puerperal sepsis.
- Premature labour, abortion, eclampsia.

On fetus:

- Congenital anomalies.
- Delivery of BIG BABIES. Macrosomia

II. Effects on pregnancy on DM:

- Gestational DM. only IGT
- Increased incidence of DKA. as pregnancy → ++ stress → ↑ant insulin

VI. OCCULAR

1. Errors of refraction.

2. Cataract.

3. Glaucoma:

close angle → ↓ drainage of aqueous
due to Rubiosis iridis (new vessel formation in the iris).

4. INFECTIONS: e.g. blepharitis & panophthalmitis.

5. Nervous: paralysis of the ocular nerves, esp. 3rd nerve.

6. DIABETIC RETINOPATHY: (earliest microangiopathy in DM)

proliferative

non proliferative

Simple Exudative

• Simple (Background) retinopathy: harmless. = diffuse pathology (damage) of retinal

• Proliferative retinopathy: neovascularization, VH, RD.

• Exudative retinopathy: macular oedema. (blurring)

neovessel formation due to ischemia of microangiopathy (hypoxia) → Growth factors

from damaged B.V. (blood vessels)

fragile B.V. → hemorrhage on retina
White Knight Love

VII. CUTANEOUS

1. Pruritus:

- Especially pruritus vulvae: due to monilial infections & parasthesia.

2. INFECTIONS:

- Multiple furuncles: & carbuncles.
- Abscesses: *localized* & *diffuse* & cellulitis.
- Fungal infections: especially in the ano-genital region & interdigital.
= *toenail pedis*

3. Diabetic dermopathy:

- 1. Nature: Red painless papules.
- 2. Site: over the shins of tibiae & may ulcerate.
- 3. Cause: occlusion of the cutaneous blood vessels. → *ischemia angiodopathy* } → *rupture of extra vasation*
Clots

Painful red
erythema nodosum

4. Necrobiosis diabetorum:

- 1. Nature: Red painless papules with yellow center.
- 2. Site: over the shins of tibiae & may ulcerate.
- 3. Cause: microangiopathy & fat deposition. ↑ LDL
↑ TG

HCO
pts & acanthosis nigricans
should be screened for
Type II DM

5. Acanthosis nigricans:

- 1. Nature: Hyperpigmented (brown to black) velvety patches.
- 2. Site: over the neck, axilla or ano-genital region.
- 3. Cause: insulin spillover into the skin (due to excess insulin in IR).

DM is
Cancer stomach
Cancer Bronchus

IR → ↑ Insulin
spillover
↓ IR

MCQ People with acanthosis nigricans should be screened for diabetes

6. Delayed healing of wounds.

angiopathy

7. Xanthomata: yellow plaques around the eye lids due to hyperlipidemia.

① to ↓

② to slow down absorption

esp cholesterol

↓ absorption of fat

8. Carotinemia: yellow discolouration of skin due to ↑↑ intake of vegetables.

9. Cutaneous features of **DIABETIC FOOT**.

*color change
trophic ulcer,
gangrene*

10. Complications of ttt: e.g. insulin lipodystrophy (see ttt).

also curly

cholesterol

*nephrotic
of
myxedema
DM*

VIII. RENAL

1. Infections:

- Urethritis, Cystitis.
- Pyelonephritis: complicated by ACUTE NECROTIZING PAPILLITIS.

2. Stones:

- More common than in normal persons. *symptomatic or even asymptomatic*

3. Diabetic nephropathy: "Diabetic glomerulosclerosis"

1. Pathology:

- ① Thickening of the BM of the glomeruli. *IG → GF*
- ② Deposition of hyaline material (sclerosis) in the glomeruli "**KW deposits**".
- ③ Disruption of part of the membrane → excessive leak of proteins. *proteinuria*

2. Clinical picture: "Kimmelstiel – Wilson syndrome"

- ① Early: **asymptomatic** with **microalbuminuria**.
- ② Later: **persistent heavy proteinuria** & **nephrotic syndrome**.
- ③ Latest: ↓ GFR, ↑ serum creatinine & **renal failure**.

- ★ **Hypertension:** is common & it causes more renal damage.
- ★ **Diabetic retinopathy:** usually precedes the development of nephropathy.

3. Investigating:

4. Treatment:

- Early: detection of **microalbuminuria** & slowing its progression to nephropathy:

- ① Strict control of DM & HTN (120/80).

- ③ ACE inhibitors.

slow down proteinuria → ↓ progress of damage

- Later: with the onset of persistent heavy proteinuria & **nephrotic syndrome**:

- ① Strict control of DM & HTN (120/80).

- ③ ACE inhibitors or ARBs.

- ④ **Diuretics for edema**
- Latest: with development of **renal failure**:

- o TTT as in uremia: renal transplantation or dialysis.

VI. ACUTE COMPLICATIONS

- COMA: "see later."

Investigating!

أوعي نكتب
nephrotic علاج
control
لأنه الكلى ترفض الدواء
idiopathic nephrotic
أعنا هذا!
Diabetic nephrotic
White Knight Love

ماتت السخى و
ويقلوه ماء

TREATMENT OF DM

LINES OF TREATMENT

- I. DIET TREATMENT.
- II. ORAL HYPOGLYCEMIC DRUGS.
- III. INSULIN.
- IV. NEW LINES OF TTT.
- V. TTT OF COMPLICATIONS.
- VI. TTT OF THE CAUSE.
- VII. TTT OF SPECIAL SITUATIONS.

I. DIET TREATMENT

CONCEPT

- To keep caloric supply in a range compatible with endogenous insulin.

CALCULATION OF DAILY CALORIES

- For underweight patients: 40 cal / Kg / day.
- For average weight patients: 30 cal / Kg / day.
- For overweight patients: 20 cal / Kg / day.

CHOICE OF DAILY CALORIES

- Carbohydrates: 50 % of calories.
- Fats: 30 % of calories.
- Proteins: 20 % of calories.

CHOICE OF CARBOHYDRATES

- Avoid simple sugars: because they are rapidly absorbed.
- Allow complex sugars: because they are slowly absorbed.

CHOICE OF MEALS

- 1 ○ Advise food rich in fibres (e.g. bran), because fibres will slow sugar absorption.
- 2 ○ Advise frequent small meals:
 - To avoid hypoglycemic attacks with insulin & oral ttt.
 - To avoid hyperglycemic peaks with large meals.

Breakfast

Lunch

Dinner

not heavy to avoid ↓

Snack to avoid ↓

II. ORAL HYPOGLYCEMIC DRUGS

1. Sulphonylureas

"Insulin secretagogues"

1 ACTION

- Decrease insulin resistance.
- Increase insulin secretion from the pancreas: **MAIN ACTION.**
- Decrease hepatic glucose production.

exhausted B cell → لا بد فقرة مؤجلة → ① قلب

insulin secretagogue

2 INDICATIONS

- NIDDM: **not** controlled on diet ttt.

3 CONTRAINDICATIONS

- IDDM.
- NIDDM: with severe hyperglycemia. → ① قلب
- DKA.
- Diabetes with pregnancy. Teratogenic. → ① II v. late
- Surgery.
- Severe liver disease or renal disease.

indications of insulin

anticoag. & preg (teratogenic)

الى م. محذوف insulin خاص

4 PREPARATIONS

Drugs	Daily dose in mg	Duration of action, hours
First generation drugs		
Chlorpropamide	100 - 500	24 - 48
Tolazamide	100 - 1000	12 - 24
Tolbutamide	500 - 3000	6 - 12
Second generation drugs		
Glimepride	1 - 8	24
Glibenclamide	5 - 15	12
Glipizide	2.5 - 40	12
Gliclazide	80 - 320	12

recent short acting

NB Second generation drugs are preferred because of shorter duration of action and therefore **less incidence of hypoglycemia.**

5 SIDE EFFECTS

- HYPOGLYCEMIA:**
- BM: depression,
- GIT: irritation.
- Skin: rash.

especially with first generation drugs.
especially with Chlorpropamide.

Aplastic anaemia

↓ G side effect
اكثر مع oral
مع insulin

NO side effect of IG

26

2. Biguanides

1 ACTION

- Increase: passage of glucose into the cells.
- Increase: anaerobic glycolysis.

- Decrease: appetite.
- Decrease: glucose absorption.
- Decrease: gluconeogenesis.

NOT insulin secretagogues

side effect → Lactic Acidosis

2 INDICATIONS

- Obese NIDDM (Type II B): (80%) not controlled on diet ttt.

3 CONTRAINDICATIONS

- Same as: Sulphonylureas.

4 PREPARATIONS

- Metformin: 500 mg tds. ^{x3}
- Phenformin: 25 mg tds (not used now). as severe lactic acidosis & may be coma

5 SIDE EFFECTS

- Appetite: loss.
- GIT: irritation. V. severe →
- Lactic acidosis. ^{anaerobic}
- Homocysteinemia. ^{low risk of atherosclerosis}
- Anemia: due to vitamin B12 malabsorption.
- ALONE: THEY DO NOT CAUSE HYPOGLYCEMIA.

أولى قبل الأكل
لازم بعد الأكل
خطا شائع أروسة

3. New oral hypoglycemic drugs

Complex sugar
α-glucosidase
Simple sugar

- a) Alpha - Glucosidase inhibitors: e.g. Acarbose.
- Decrease post prandial hyperglycemia by: delaying glucose absorption.

- b) Benzoic acid derivatives: e.g. Repaglinide.
- Increase INSULIN SECRETION. V. potent secretagogue

- c) Insulin sensitizers: "Thiazolidine-diones" e.g. Rosiglitazone & Pioglitazone.
- Decrease INSULIN RESISTANCE (PPARγ agonists).

PPAR-γ
Peroxisome
Proliferator
Activated
Receptor
= receptor molecules intracellular (nuclear)
this drugs binds to them

- ① upregulate insulin receptors (S.U.)
- ② improves intracellular enzymatic Rx (post receptor)

P PPAR Gamma

WhiteKnightLove

III. INSULIN

INDICATIONS

- **IDDM.**
- **NIDDM:** with severe hyperglycemia not controlled by diet & OHD.
- **DKA.**
- **Diabetes with pregnancy.**
- **Surgery.**
- **Severe liver disease or renal disease.**
- **Severe stress:** infection. *due to anti-insulin release*

ORIGIN

- **Animal insulin:** from cows or pigs rarely used now.
- **Human insulin:** genetic engineering widespread use now: most powerful, least allergic.

PREPARATIONS

Insulin	Onset	Peak	Duration
Short acting			
Crystalline (regular)	½	3	6
Semilente	1	6	12
Intermediate acting			
Isophane (NPH)	3	8	24
Lente	3	8	24
Long acting			
Protamine zinc insulin	4	16	36
Ultralente	4	16	36
Mixtures	Mixtard: 30 / 70 & Initard: 50 / 50		

DOSE

- The ttt is usually started with 20 units / day in average weight patients.
- The dose is gradually increased (e.g. by 5 - 10 units / day) until blood glucose is controlled.
- The dose is maintained for life & monitored

لا يتغير الجرعة عادةً للتغيير حسب لوزنهم أو جسم

طالما بقيت أنسولين

every 3w → Blood glucose
every 3M → glycosylated HbA1c

by: daily
Blood glucose 6 times / d
قبل وجبة أو وجبات

White Knight Love

سؤال عام
= clinical uses = indications + Hyperkalemia
أكبر علاج للسكر

insulin up → ↑ incidence of Insulin resistance

Abs

obsolete cheap

(no incidence of Insulin resistance)

- ① Brittle (fluctuant)
- ② Newly diagnosed hyperglycemic pt
- ③ Diabetic Coma or hyperosmotic Coma
- ④ Surgery

pt poorly controlled

oral

قاعدة

short: is used when DM is poorly controlled
السكر غير خاضع للتحكم

max 24h
لا

not by: HbA1c
لا يتغير

dinner

lunch

Breakfast

لا يتغير الجرعة عادةً للتغيير حسب لوزنهم أو جسم

short

long

ADMINISTRATION

A SUBCUTANEOUS:

Many methods could be used, e.g.

1. Single injection before breakfast:

"Mixtard"

- Short acting (30 % of the required dose) + long acting (70 % of the required dose).

2. Twice daily injections:

"Long"

- Morning injection: $\frac{2}{3}$ of the total daily dose.
- Evening injection: $\frac{1}{3}$ of the total daily dose.

eg 60 units
 $\frac{2}{3}$ every
 $\frac{1}{3}$ every

3. Multiple daily injections: "in cases of poor glycemic control"

- Regular insulin before each meal + evening long acting insulin.

NB Injections can be given by insulin syringes or by pen injection devices.

قلم وحقنة من الأنسولين وحقن الودعات بغير حقنة وحقنة

- 1. Economical
- 2. Painless
- 3. Used by blind PT (Retinopathy)

4. Continuous Subcutaneous Insulin Infusion:

Insulin pump

They deliver: **rapid-onset, short-acting insulin** 24 hours a day,
 Through a: **catheter placed under the skin.**

DOSES:

- **Basal** (small) dose: delivered constantly.
- **Bolus** dose: delivered with meals.

ADVANTAGES:

- Eliminates the need for injections.
- Delivers insulin more accurately than injections.
- Decreases the fluctuations in blood glucose levels.
- Decreases the episodes of hypoglycemia.
- Allows more flexibility with meals.

DISADVANTAGES:

- Expensive.
- Inconvenient.
- DKA: if the catheter comes out & there is no insulin for hours.

B IV infusion or IM:

In case of DKA or Hyperosmolar coma.

C Insulin spray (Nasal or Oral):

New.

D Oral insulin:

Investigational.
 as its bioavailability by GIT (nil)

Oral
 anti-insulin
 night, day, evening
 كثير الصبح
 معانزها قليلة بالليل
 خاف من nocturnal hypoglycemia

Break Launch Dinner
 ↑ ↑ ↑
 S S S
 Long
 لقاح ثاني يوم الصبح



جهاز
 وقطر
 تحت الجلد

مكتفاه لما يأخذ دس لازم يحوت
 DKA لو ناموا اخلت

غير انه ساعات
 long

لا يقل لغاية

breakfast ثاني يوم
 لقاح متدايم بموافقاني (الخبره)

COMPLICATIONS

1. HYPOGLYCEMIA.

2. Weight gain. $E \begin{cases} \uparrow \text{lipogenesis} \\ \downarrow \text{lipolysis} \\ \uparrow \text{appetite} \end{cases}$

3. Insulin lipodystrophy: atrophy of SC fat at sites of injections forming skin dimples.

4. Allergic reactions: least with human insulin. $\uparrow$ animal

5. Insulin resistance: due to:

- Antibodies against insulin preparations (least with human insulin). $\uparrow$ animal
- Obesity. $++$ fat cells $\rightarrow ++$ IR $\rightarrow$ احتياج جرعات أكبر $\rightarrow$ على المدى الطويل $\rightarrow$ Oral

6. Insulin in a wrong dose: "Night Dose"

- Dawn phenomenon: morning hyperglycemia due to under dosage of insulin.
- Somogyi effect: morning hyperglycemia following nocturnal hypoglycemia due to over dosage of insulin.

HONEYMOON PHASE

- A TEMPORARY phase in the first 1 – 2 years after the onset of TYPE I DM.
- Reduction in exogenous insulin needs due to temporary improvement in β cell function.
- Blood glucose is controlled with very small doses of insulin.

IV. NEW LINES OF TTT

- Pancreatic transplantation.
- Pancreatic islet cells transplantation.

V. TTT OF COMPLICATIONS

chronic e.g. TTT of diabetic nephropathy: see before.

acute e.g. TTT of different types of coma: see later.

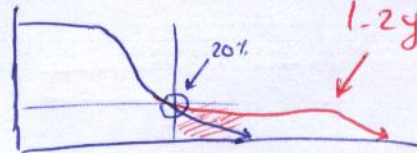
DICA

VI. TTT OF CAUSE (in secondary D)

e.g. TTT of CRF.

diagnosis

White Knight Love



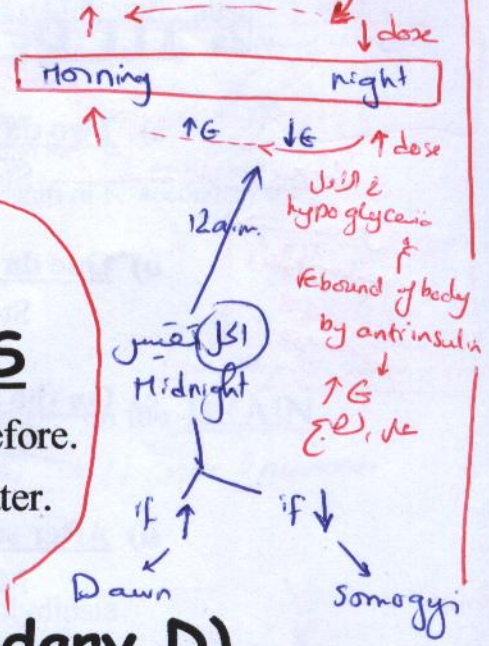
عده ايسنة ← الحياه محتاج انولين
أفضل سويه

خفر

خطأ
مريض جيد الدكتور
under

Oral
لم تنزود
المجرعة على
المدى الطويل

Oral



وتقول طابا انه
يبقى معكم نزل جرعة بالليل
لانه معكم يكون
وانت مستعاطن
White Knight Love

VII. TTT OF SPECIAL SITUATIONS

1. TTT OF DM DURING PREGNANCY

SQ

a) General:

Daily home blood glucose monitoring + outclinic assessment every 2 weeks.

b) Investigations:

Fundus exam. + urinary protein at first, at 28 weeks & before delivery, because *retinopathy* & *nephropathy* may deteriorate during pregnancy.

(eclampsia)
is predisposed by DM

c) Control:

By diet ttt, if not enough, give insulin.

Oral hypoglycemic drugs are contraindicated.

Teratogenic
Antistress

SQ

2. TTT OF DM DURING SURGERY

لوعلى
cholecystitis
DM

لازم جراح و اعلى

a) Two days before surgery:

لو هو مريض
الحي على
الاول حاجه
48 ساعة
توقفه مريض
Stop: oral hypoglycemic drugs.

b) One day before surgery:

Stop: long acting insulin & replace by: short acting insulin.

c) On the surgery day:

Give: infusion of glucose, short acting insulin & K. → as ↓ K
anhydrous

d) After surgery:

Maintain: the infusion until the patient is allowed to eat.

e) Monitoring:

intra & post opent
Check: glucose & K levels every 4 hours.

تم ترجع للعلاج الى كانه مريض عليه قبل الجراح

إندوكرين
endocrine

COMA IN DM

I. DIABETIC KETOACIDOSIS (DKA)

"Diabetic coma"
Acute condition
on top of chronic

- DKA is the hallmark of TYPE I DM. (DKA prone)

ETIOLOGY

- **Stoppage of insulin intake** (missed insulin). *adequate but ↑ G diet*
- **Severe hyperglycemia** (inadequate tt). *inadequate from start*
- **Stress of a precipitating factor:** *which needs high energy as in:*
 - Psychological stress.
 - Pregnancy, labour.
 - Stroke, AMI.
 - Surgery, Infection, Trauma.

antinsulin!!

PATHOGENESIS

(absolute insulin deficiency)

1. Insulin: very low → hyperglycemia → osmotic diuresis (polyuria) → **Dehydration**.

2. Fats: Lipolysis to produce energy → ↑↑ ketone bodies which will cause:

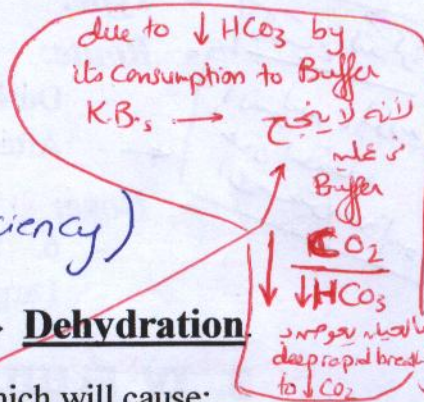
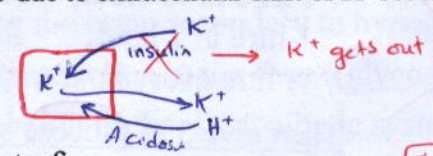
- Ketonemia → **Metabolic acidosis**.
- Ketonuria → acetone in urine.

ربط بين السكر و ketone

3. Potassium: **Hyperkalemia** occurs due to extracellular shift of K secondary to:

- Insulin deficiency.
- Acidosis.

oral normal total body K or low if severe osmotic diuresis



4. COMA: due to the combined effect of:

Dehydration, Acidosis, & Hyperkalemia on the **BRAIN**.

shrinkage (hypertonic) encephalopathy → ↓ cortical neurones

CLINICAL PICTURE

1. General: Slow onset with marked Polyuria + Polydipsia. *hours to days*
2. GIT: Dyspepsia, nausea, vomiting, + acute abdominal pain. *asymptomatic*
3. Breath: Rapid deep breathing (Kussmaul's) + acetone odour.
4. Brain: Confusion, then Coma. (dehydrate, Acidosis, HyperK⁺)
5. Dehydration: Dry skin, dry tongue, sunken eyes, + weak rapid pulse, ↓ BP. *hypovolemic shock*

hypoglycemia (minutes)

hypoglycemia عرقانة

White Knight Love

Q Management DKA : Pathogens / CIP / investig / ttt
(25M) then after control of DKA DM علاج DM

(Contra indication) Diet . Insulin . لو كبت oral hypoglyc

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INVESTIGATIONS

1. Blood: Glucose is markedly increased.
2. Urine: Glucose & acetone appear in urine. → DKA
3. Serum K: Increased (extracellular shift).
4. pH: Decreased. $\bar{e}$ Total body K either Normal or ↓ if severe osmotic diuresis
5. Serum Na: $HCO_3^- \downarrow$ (arterial) Increased due to concentration by dehydration

TREATMENT

1. HOSPITALIZATION:

better in an ICU.

2. INSULIN:

- Type: short acting insulin.
- Route:
 - During ketosis: $\rightarrow$ steady control
 - After disappearance of ketosis: Multiple daily SC injections.
- Dose:
 - 6 – 10 units / hour: until ketosis disappear.
 - Larger doses (12 – 20 units / hour): may be used in resistant cases.

3. IV FLUIDS:

- Amount required: usually 4 – 8 litres.
- Type:

- Start by normal saline as follows:

1 litre in $\frac{1}{2}$ hour, followed by:
1 litre in 1 hour, followed by:
 $\frac{1}{2}$ litre every hour until the deficit is replaced.

- Then give 5 % glucose solution:

When blood glucose drops to 250 mg / dl: to avoid hypoglycemia.

4. CORRECTION OF ACIDOSIS:

- IV infusion of sodium bicarbonate: in severe acidosis (pH < 7.1).
[if $HCO_3^- \downarrow < 10 \text{ mEq/L}$]

5. POTASSIUM:

Should be given because:

- Hypokalemia occurs during ttt due to intracellular shift of K secondary to:
 - Insulin therapy.
 - Correction of Acidosis.
- Dose: 20 – 40 mEq of K added to each litre of infusion.

guided by serum K

6. TTT OF THE PRECIPITATING FACTORS:

- e.g. Antibiotics for infection.

7. MONITORING OF THE PATIENT

• Clinically:

- Level of consciousness. → Glasgow Coma Scale
- Signs of dehydration.
- PULSE, BP & CVP. إم حارة

• Laboratory:

- Blood: Glucose.
- Urine: Glucose & acetone.
- Serum K.
- pH.

II. HYPOGLYCEMIC COMA

ETIOLOGY

- Over dose of insulin or sulphonylurea.
- Diminished carbohydrate intake following ttt: missed meal.

Not Biguanides as not secretagogues

PATHOGENESIS

- Coma: due to ↓ energy supply to the brain secondary to hypoglycemia.
- Adrenaline: is secreted to ↑ glucose production in the liver (glycogenolysis).
- Hyperadrenalism: occurs & causes stimulation of the sympathetic system.
↑ catecholamines

CLINICAL PICTURE

- There are features of:

“Sympathetic over activity”

- Symptoms: Rapid onset of Irritability, tremors, pallor, sweating, palpitation.
- Signs: Dilated pupils, moist skin, strong rapid pulse, ↑ BP.
- Course: Convulsions, Coma, Brain damage & death in severe cases.
- Response to ttt: Rapid response to IV or oral glucose.

Sympathetic

brain death حالة حادة قبل

لوحظت
تغيرت عليه

أو ما يسمى
بالحرق
والرعدة

كثرة

DKA
Slow

DKA
Sunken eye
dry
weak
↓ BP

INVESTIGATIONS

1. Blood: Glucose is markedly decreased ($< 50 \text{ mg / dl}$).
2. Urine: No glucose in urine.

TREATMENT

1. In severe hypoglycemia: IV glucose & IV glucagon (in resistant cases).
2. In early hypoglycemia: oral glucose.

antinsulin → ~~glycogenolysis~~
→ Glucose

	DKA	Hypoglycemia
1. History	Missed insulin	Missed meal
2. Onset	Slow	Rapid
3. Coma	Silent	Irritable
4. Skin	Dry	Moist
5. Tongue	Dry	Moist
6. Eyes	Sunken	Normal
7. Pupils	Normal	Dilated
8. Respiration	Kussmaul's	Normal
9. Breath	Acetone odour	Normal
10. Pulse	Weak & rapid	Strong
11. BP	Low	High
12. Urine	Glucose & acetone	Normal
13. Blood glucose	Very high	Low
14. Response to glucose	No effect	Rapid improvement

لو واحد ز العرا وعنده غيبوبة و ساطع

مبدأ ادى جلوكوز

لأنه لو كانه $\downarrow G \rightarrow$ غيبوبة
ولو كانه DKA $\leftarrow 1000$ من غيبوبة معاه

Relative Insulin Deficiency

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III. HYPEROSMOLAR NON-KETOTIC COMA

Severe hyperglycemia without ketosis, usually in a neglected elderly TYPE 2 DM.

ETIOLOGY

1. Uncontrolled Type 2 DM: with severe hyperglycemia.
2. A precipitating factor such as: Stroke, AMI, or infection.

PATHOGENESIS

1. Insulin deficiency is less severe in Hyperosmolar coma than in DKA.
2. Low endogenous insulin → hyperglycemia → osmotic diuresis → Dehydration.
3. Low endogenous insulin: is sufficient to inhibit ketogenesis → no Acidosis.

Concentrated Na
Hyper osmolar

CLINICAL PICTURE

"Dehydration with no acidosis"

1. General: Slow onset with marked Polyuria + Polydipsia.
2. Brain: Confusion, then Coma. (due to dehydration only not Acidosis)
3. Dehydration: Dry skin, dry tongue, sunken eyes, + weak rapid pulse, ↓ BP.

no GIT / no

INVESTIGATIONS

1. Blood: Glucose is markedly increased, ↑ Na (due to dehydration).
2. Urine: Glucose appears in urine, BUT no acetone.

TREATMENT

1. Hospitalization: better in an ICU.
2. IV fluids: using normal saline
3. Insulin: as in DKA.
4. Potassium: as in DKA.
5. Na Bicarbonate: is not given.
6. TTT OF THE PRECIPITATING FACTORS: e.g. Antibiotics for infection.
7. Monitoring the patient: as in DKA.

"The most important measure"

no add fluids to normal saline
insulin 2 units/hr

no need for pH monitoring as no ~~D~~ Acidosis

IV. LACTIC ACIDOSIS COMA

حتى لو اسكر
عنا

ETIOLOGY

- It occurs in diabetics using **BIGUANIDES**.
- It may be precipitated by **TISSUE HYPOXIA**, e.g. **HF** (shock, resp. failure).
- BIGUANIDES** or **TISSUE HYPOXIA** → Anaerobic glycolysis.
- Anaerobic glycolysis → accumulation of lactic acid → severe **Acidosis**.

anaerobic → L.A. Pyruvic acid

و طواينه
benfennie

ppt by DM

CLINICAL PICTURE

"Acidosis with no dehydration"

- Breath:** Rapid deep breathing (Kussmaul's) ~~acetone odor~~ PH ↓
- Brain:** Confusion, then Coma.

Investig: ↓PH

TREATMENT

- IV sodium bicarbonate.

Hyperparathyroidism
is not the only cause of TCa

PTH ↓ serum P
↑ serum Ca

control
vit D
so, ↓ serum Ca

- intestine: ↑ absorption (act. vit D)
- Kidney: ↑ reabsorption, & ↑ excretion of P
- Bone: ↑ resorption (osteoclastic activity)

* functions of Ca:

- Mus contraction (actin over myosin)
- Neuromuscular transmission
- Bone & teeth
- Coagulation system

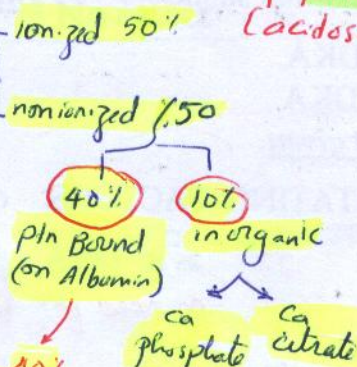
* Normal Levels

total Ca : 8.5 - 10.5 mg/dl
P : 2.5 - 4.5 mg/dl

- * ↑ Ca & ↑ P = Acromegaly
- * ↓ Ca & ↓ P = malabsorption

نمنا كذا الحادى الرقتل
ده تزود ده العكس

albumin ضرورى
nephrotic
serum Ca normal
also Albumin must be normal



if pH normal 50% ionized
50% non "

if pH ↑ (alkalosis) ionized ↓
if pH ↓ (acidosis) ionized ↑

pH
ماتوسلانية
total
(لاغير)

shift
فقط
ionized
& non "

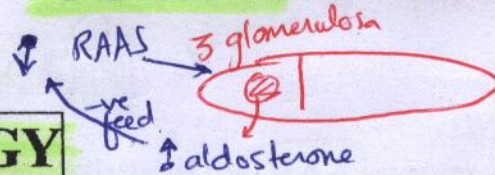
TBD, DM, parathyroid
→ Kidney stones

PRIMARY HYPERALDOSTERONISM SP

"CONN'S SYNDROME"

ETIOLOGY

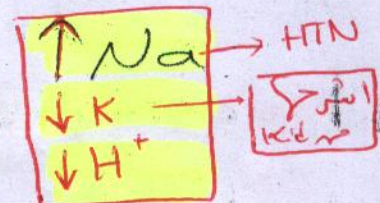
1. Adrenal adenoma: the most common cause.
2. Adrenal hyperplasia: bilaterally.



*↑ aldosterone
↓ renin activity by
-ve feedback.*

CLINICAL PICTURE

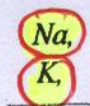
1. Hypertension: may be severe & malignant.
2. Hypokalemia: see "kidney".
3. Metabolic alkalosis: see "kidney".
4. Polyuria: *hypokalemia - sensitivity of renal tubule to effect of ADH*



INVESTIGATIONS

1. Blood Chemistry:

- Increased:
- Decreased:



due to metabolic alkalosis

HCO₃⁻ ↑

Aldosterone.

Plasma rennin activity

-ve feed

2. Imaging:

- CT & MRI: abdomen will differentiate between adrenal tumours & hyperplasia.

3. ECG:

- Evidence of Hypokalemia: see "Kidney".

TREATMENT

1. For adenoma: surgical removal.
2. For hyperplasia: spironolactone 100 - 400 mg daily (K - sparing diuretic).

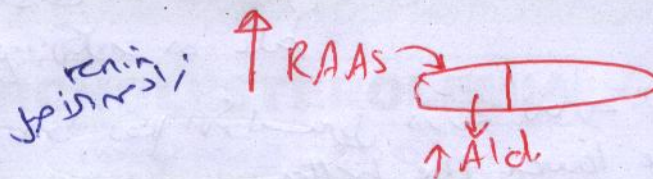
*aldosterone antagonist
& treats also HTN] double effect.*

SECONDARY HYPERALDOSTERONISM

SP

1 DEFINITION

- It is an increased activity of the **RAA** system.



2 ETIOLOGY

Renin overproduction:

- Accelerated & Malignant hypertension.
- Renal artery stenosis.

renal damage
renal ischaemia
hypoxia

↑ renin

Hypovolemia:

- Heart failure.
- Liver failure.
- Nephrotic syndrome.
- Excess diuretics.

renal hypoxia

Extravascular edema
volume ↓ B.V. → G.F.

3 C/P as 1ry hyperaldosteronism (Conn's)

4 INVESTIGATIONS

- Increased: Plasma rennin activity, Plasma Aldosterone.
- Serum Na: may be low in cases of Hypovolemia.

Conn's
(↓)

↑ ACTH
Cushing's

5 TREATMENT

- ACE inhibitors.
- Spironolactone. aldosterone antagonist
- TTT of the cause. eg H.f. : digitalis

stop renin
stop Aldosterone

Oral 1000

63

DISORDERS OF LIPID METABOLISM

N: 150-200 mg/dl

normally cholesterol not more than

HYPERCHOLESTEROLEMIA

200 mg/dl

1. Primary:may reach 1000
Familial Hypercholesterolemia (FH).

→ most common cause of stroke & coronary in young age

2. Secondary:

- Hypothyroidism.
- Obstructive jaundice. *normal esterification*
- Nephrotic syndrome.
- Acute intermittent porphyria. *inborn error in haeme metabolism*
- DRUGS: *Thiazide diuretics, Cyclosporine. @ associated inborn error in lipid metabolism*

HYPOCHOLESTEROLEMIA

1. Malnutrition, Malabsorption.

2. Hyperthyroidism.

3. Chronic infections:

*AIDS, TB.**Catabolic on cholesterol***HYPERTRIGLYCERIDEMIA**

1. Metabolic:

*DM**CRF**→ the most common cause*

2. Obesity.

3. Alcoholism.

*→ apolipoprotein inhibition*4. DRUGS:*Thiazide diuretics,**Estrogen,**Beta adrenergic blockers.***COMBINED HYPERLIPIDEMIA**

1. Hypothyroidism.

2. Nephrotic syndrome.

3. Thiazide diuretics.

• ↑ cholesterol dangers: { Brain
heart
B-v.

• ↓ cholesterol: زمان كانوا فاكرين له خطورة
{ ↑ incidence cancer
psychiatric disturbance
دلو قى طلع الكلا ده غلام

لذلك لما ندى دوا يقل الكوليسترول ندره لغاية اى ندى؟
the lower the better

• ttt for ↑ cholesterol:

- Statins * ↓ HMG Co-A Reductase
Hydroxy Methyl Glutaryl
so, ↓ synthesis of cholesterol

* side effect: - on H.S & liver
- compensatory ↑ in ~~synthesis~~ absorption

- Ezetimibe: * ↓ absorption
* side effect - compensatory ↑ in synthesis

statin + Ezetimibe
in v. severe ↑ cholesterol

دوا اى
Inegy → avoids compensatory rise
ما يلى
ما على جات

• ttt for ↑ TG:

- Fibrates

• ttt for combined → Ch: 400
TG: 1600 زيغ
fibrates (مع) statin or Inegy لا ينفج اى

والا ضايع ال liver

الكل اعلاج واحد وبعده واحد

اعلاج من الاول؟ مبعأ

Oral 1000

TG النعل

الهدف من علاج اى افعل
LDL

N: 130 mg/dl

عائز نزل عن 130

واو الناس high risk

عائز نزل عن 100

v. recently

قله الى 70

لانه هو العيان من هيجل stroke الزرقة
acute TG نعل حاجه acute
Hypertiglyceridemia → Acute pancreatitis

White Knight Love
TG و يجرش حاجه نه cholesterol سببه مؤقتاً سون